REVIEW on PhD Thesis
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RESEARCH ON THE BIOCHEMICAL AND LABORATORY ANALYSIS CHANGES IN NEWBORN BABIES WITH ESOPHAGEAL ATRESIA

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Abstract. Objective. The main objective of this research theme was to determine the biochemical and laboratory analyzes changes in newborns with esophageal atresia.
Material and methods. For wet biochemistry analyzes assessing apparatus was used Hitachi 717 and 917. To obtain results for the dry biochemistry has been used Ektachem-Vitros 250 analyzer, and for determining the blood counts and the Sysmex SF-3000 systems were used, and D-Cell 60. For protein electrophoresis, electrophoresis system was used. In the study were evaluated in terms of analytical results (biochemical lab) 15 patients born with esophageal atresia. Add to this a total of 30 cases of healthy newborns, considered the control group. For the both group laboratory analyzes were collected immediately after their birth specifying that the lot of cases maneuver was performed prior to surgery malformation correction to detect and correct the presence of amendments parameters examined.
Results. In all cases studied in 15 cases with esophageal atresia, 14 cases had lower values of protein level, 6 patients was low blood sugar, 7 patients newborns had low lipemia, direct bilirubin and total bilirubin was increased to a total of 13 patients, 5 patients had higher values of the blood urea and TGP's, 11 patients had hypocalcemia. The purpose of this paper is to emphasize that a correct diagnosis and early performed immediately after birth, followed by metabolic imbalances of electrolyte and acid-base imbalances, correcting hypoxia and establishment of specialized surgical treatment cases with good prognosis ensure patient survival with a normal life later.

Key words: Esophageal atresia, lower tracheoesophageal fistula, upper cul de sac, hypoglycemia, hypoproteinemia.

Introduction

The esophageal atresia is a congenital anomaly represented by interrupting the continuity of the esophagus and it is the type of malformation incompatible with life, but that healing can be achieved without sequelae in favorable cases (Tica şi Enache, 2013). In Romania the frequency of esophageal atresia is estimated to be 1 in 5,000 births, but unfortunately there are areas in our country where this condition is unknown or diagnosed late (Tica, 2001).

The diagnosis of esophageal atresia is antenatal and postnatal. Antenatal diagnosis of esophageal atresia is often difficult due to the presence to the following elements: hydramnios, prematurity and low volume ultrasound absence or atresia of type II gastric pouch and upper esophageal dilatation sac (Sabetay, 2008; Sabetay şi col., 2004; Tica şi Enache, 2013). Postnatal diagnosis of oesophageal atresia is based on the following: probe radiographs radio-opaque probe, thoraco-abdominal radiographs, take stock of associated malformations (VACTERLL syndrome) (Sabetay, 2008; Sabetay şi col., 2004; Tica şi Enache, 2013).

The main objective of this research theme was to determine the biochemical and laboratory analyzes in esophageal atresia in neonates. The study was conducted during 1.01.2005-31.12.2011 in the Neonatology department and Pediatric Surgery Clinic of Clinical Emergency Hospital "St. Andrew" of Constanţa.

The Purpose of this paper is to emphasize that a correct diagnosis and early performed immediately after birth, followed by metabolic imbalances (correction hypoproteinemia, hypoglycemia, lipid-lowering), electrolyte and acid-base imbalances and establishing specialized surgical treatment in cases with good prognosis ensure patient survival with a normal life. Index esophageal atresia healing is 80-90 % in the western countries. If in cases of unfavorable treatment is difficult, requiring complex therapeutic means, favorable cases should heal without sequelae. Hence the need for early diagnosis of pulmonary lesions before instalation. This diagnosis is possible in our country in maternity immediately after childbirth. It is very important is to check the patency of the esophagus which exam should be part of the initial assessment of all newborns.

Material and methods

Apparatus used in the laboratory. For wet biochemistry analyzes assessing apparatus was used Hitachi 717 (Figure 1) and Hitachi 917 (Figure 2).

Figure 1. Apparatus Hitachi 717

Figure 2. Apparatus Hitachi 917.

To obtain results for the dry biochemistry has been used Ektachem-Vitros 250 analyzer (Figure 3), and for determining the blood counts and the Sysmex SF-3000 systems were used (Figure 4), and D. Cell 60 (Figure 5).

Figure 3. Analyzer Ektachem-Vitros 250

Figure 4. Apparatus Sysmex SF3000

Figure 5. Apparatus D Cell 60

For protein electrophoresis, electrophoresis system was used.

Table 1 showed normal values of the biochemical parameters analyzed in the cases studied.

Table 1. Normal values of the characteristics sought.

Marker	Normal values newborn	Marker	Normal values newborn
Total Proteine	6-8 g/100 ml	Ca	9 – 11 md/dl
Albumin	3,64-4,34 g/100 ml	Na	135 – 148 mmol/l
Globuline	2,66-3,36 g/100 ml	Cl	98-110 mmol/l
α1-globulin	0,14-0,35 g/100 ml	K	3,5 -5,9 mmol/l
α2-globulin	0,42-0,63 g/100 ml	CBC	
β-globulin	0,56-0,77 g/100 ml	Leukocytes	5.000-20.000/mm^3
γ-globulin	0,98-1,47 g/100 ml	Lymfocytes	0,8 - 4 x 10^3/mm^3
		Myelocytes	0,1 - 0,9 x 10^3/mm^3
Blood Glucose	60 -99 mg/dl	Granulocytes	2- 7 x 10^3/mm^3
Total Lipids	600-800 mg/100 mL	Erytrocytes	3,9– 5.9 x 10 6/ mm^3
Serum Cholesterol	120 - 200 mg/dl	Hemoglobin	13,4 – 19,8 g/dl
HDL Cholesterol	45 – 85 mg/dl	Hematocrit	41 - 65 %
LDL Cholesterol	< 130 mg/dl	MCV	82 - 95 fL
Triglycerides	30 -135 mg/dl	MCH	27 - 31 pg
Direct Bilirubin	0 - 0,2 mg/dl	MCHC	32 - 36 g/dl
Total Bilirubin	0 – 1,2 mg/dl	RDW-CV	11,5 - 14,5%
Urea	10-50/mg/dl	RDW-SD	35 – 56 fL
Creatinine	0,6-1,1 mg/dl	Platelets	150000–300000/mm3
Uric Acid	2,6 - 6 mg/dl	MPV	7 -11 fL
TGP	< 50 UI	PDW	15-17 fL
TGO	< 54 UI	PCT	0,108 – 0,282%
Acid phosphatase	10,4 – 16,4 UI/l	Sideremie	50 -160 µg/dl
Alkaline phosphatase	50 - 275 UI/l		

The studied group. In the study were evaluated in terms of analytical results (biochemical lab) 15 patients born with esophageal atresia. Add to this a total of 30 cases of healthy newborns, considered the control group. For the both group laboratory analyzes were collected immediately after their birth specifying that the lot of cases maneuver was performed prior to surgery malformation correction to detect and correct the presence of amendments parameters examined.

Results and discussion

Descriptive analysis of cases

Diagnosis. Complete diagnosis of newborn patients in the study is shown in Table 2.

Table 2. Complete diagnosis for the 15 cases

The Diagnostic	Frequency	Percent	Valid Percent	Cumulative Percent
Esophageal atresia type I, plurimalformative syndrome, prematurity, incipient respiratory distress syndrome.	2	13.3	13.3	13.3
Esophageal atresia type III with lower tracheo-oesophageal fistula, aspiration bronchopneumonia, right pneumothorax, prematurity.	1	6.7	6.7	20.0
Esophageal atresia type III with range lower tracheo-oesophageal fistula, high ano-rectal malformation, aspiration bronchopneumonia, prematurity, respiratory distress syndrome.	1	6.7	6.7	26.7
Esophageal atresia type III, high ano-rectal malfor-mation, cardiovascular malformation, prematurity	1	6.7	6.7	33.3
Esophageal atresia type I, prematurity	3	20.0	20.0	53.3
Esophageal atresia type I, anal imperforation, prematurity	1	6.7	6.7	60.0
Esophageal atresia type III, with lower tracheo-oesophageal fistula	5	33.3	33.3	93.3
Esophageal atresia type III with lower tracheo-oesophageal fistula, plurimalformative syndrome, prematurity	1	6.7	6.7	100.0
Total	15	100.0	100.0	

The total number of births. The Neonatology Department of Clinical Emergency Hospital "St. Andrew" Constanţa the total number of births in the period 1.01.200 -31.12. 2011 was 31.343 (Table 3).

Table 3. The number of births registered in Constanta County Hospital during 2005-2011

	2005	2006	2007	2008	2009	2010	2011
Total births of which	5230	4974	4935	5373	4411	3633	2787
Urban	3794	3413	3357	3925	2982	2494	1852
Rural	1436	1561	1578	1448	1429	1139	935
Male	2802	2594	2764	3009	2162	1671	1441
Female	2428	2380	2171	2364	2249	1962	1346

Distribution of cases. Distribution of cases with esophageal atresia recorded in Clinical Emergency Hospital "St. Andrew" Constanţa during 2005-2011 is shown in Figure 6.

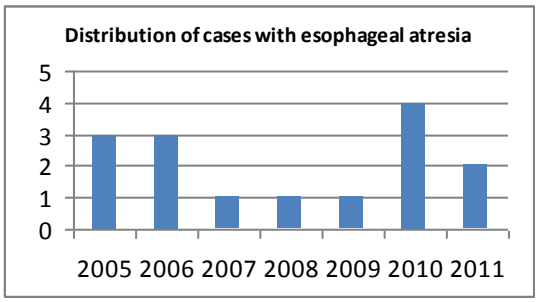

Figure 6. Distribution of cases with esophageal atresia during 2005 – 2011

The risk of death

We calculated the risk of death (until discharge) neonates with esophageal atresia compared with existing risk in the general population (Table 4).

Table 4. Table contingency risk death
(esophageal atresia children - children without esophageal atresia)

		Efect		
		+	-	Total
Exposure	+	6	9	15
	-	265	31063	31328
	Total	271	31072	31343

Analysis of the main biochemical and hematological markers

Total proteins. In patients with esophageal atresia, the minimum recorded value of the total protein is 3.82 g/100ml and the maximum value is 7.68 g/100ml (Table 5).

Table 5. Descriptive analysis of total protein

Descriptive Analysis

Total Protein

Lot	N	Mean	Std. Deviation	Minimum	Maximum	Median
Case	15	5.1047	.89597	3.82	7.68	4.9100
Witness	30	6.6727	.37060	6.12	7.45	6.5600
Total	45	6.1500	.95117	3.82	7.68	6.4200

Figure 7. Box-plot type is observed that except one case, which is considered to be an exception (outliner), all neonates with esophageal atresia presents lower values of this marker **compared to those of control** group (Beiu et al 2013).

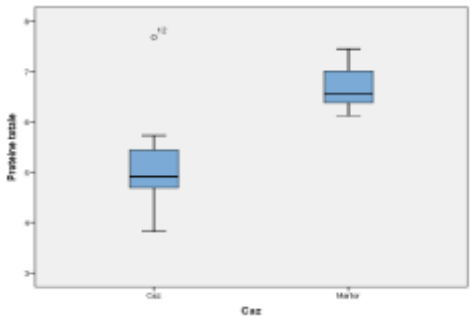

Figure 7. Distribution of the total protein values (Beiu et al 2013).

Of the total number of cases studied, 14 cases had hypoproteinemia. For thelot of cases distributions of blood proteins do not follow a normal distribution (Table 6).

Table 6. Testing normality of the distribution of values of total protein

Normality tests

	Lot	Kolmogorov-Smirnov[a]			Shapiro-Wilk		
		Statistic	df	Sig.	Statistic	df	Sig.
Total protein	Case	.176	15	.200*	.866	15	.029
	Witness	.140	30	.139	.948	30	.154

*. This is a lower bound of the true significance.

a. Lilliefors Significance Correction

The null hypothesis claims that total protein values did not differ between the two groups. This hypothesis is rejected at a level of statistical significance at $p<0.001$.

So there are statistically significant differences between total protein values recorded in neonates with esophageal atresia and the same indicator in neonates in the control group (Table 7).

Table 7. Mann-Whitney test for total protein

Test Statistics[a]

	Total Protein
Mann-Whitney U	30.000
Wilcoxon W	150.000
Z	-4.698
Asymp. Sig. (2-tailed)	.000

a. Grouping Variable: Lot

Glucose. The lowest value was 24 mg / dl, which was identified in one case, and also the largest value has been identified for a newborn esophageal atresia, which is 343 mg/dl. For the control group, all values were within normal limits. In the cases of all studied 15 patients with esophageal atresia, 6 patients blood glucose was reduced (Table 8).

Table 8. Descriptive analysis of the blood glucose values

Descriptive analysis

Blood glucose

Lot	N	Mean	Std. Deviation	Minimum	Maximum	Median
Case	15	74.93	78.573	24	343	51.00
Witness	30	90.63	9.557	77	109	90.00
Total	45	85.40	45.614	24	343	88.00

To graphically view how are distributed the glycemia values, was achieved chart type box-plot (Figure 8) from which it appears that a case has a value considered outliner (Roşoiu et al, 2013).

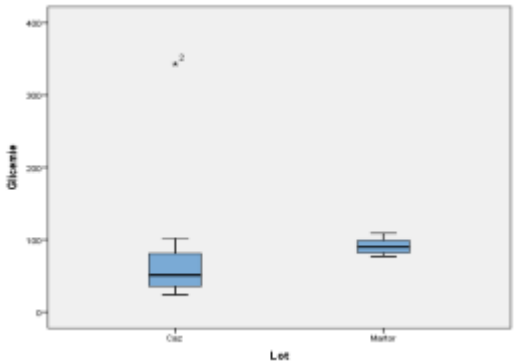

Figure 8. Distribution of the blood glucose values (Roşoiu et al, 2013)

Distribution of blood glucose control group did not follow a Gaussian distribution. In order to test the statistical significance of the differences between the two groups was used Mann-Whitney U test (Table 9).

Table 9. Testing blood glucose normality distribution

Normality tests

	Lot	Kolmogorov-Smirnov[a]			Shapiro-Wilk		
		Statistic	df	Sig.	Statistic	df	Sig.
Blood glucose	Case	.299	15	.001	.585	15	.000
	Witness	.090	30	.200*	.947	30	.144

*. This is a Limita inferioară bound of the true significance.
a. Lilliefors Significance Correction

After applying the Mann-Whitney test showed that there is a significant difference statistically between blood glucose levels in patients with esophageal atresia and those in the control group (p = 0.002) (Table 10).

Table 10. Mann-Whitney test for Blood Glucose

Test Statistics[a]

	Blood Glucose
Mann-Whitney U	98.000
Wilcoxon W	218.000
Z	-3.059
Asymp. Sig. (2-tailed)	.002

a. Grouping Variable: Lot

Total Lipids. In the lot of cases studied minimum values of the total lipids in the blood was 72 mg/dl well below normal minimum. Of the 15 cases with esophageal atresia studied, a total of 7 patients newborns had low lipemia, who are preterm (Table 11).

Table 11. Descriptive analysis of total lipids values

Descriptive analysis
Total lipids

Lot	N	Mean	Std. Deviation	Minimum	Maximum	Median
Case	15	530.60	200.910	72	765	596.00
Witness	30	696.40	56.147	611	798	682.00
Total	45	641.13	145.495	72	798	671.00

The box-plot in Figure 9 is rendered graphically descriptive data analysis. It is noted that there are two values considered among cases (much lower values compared to the other values).

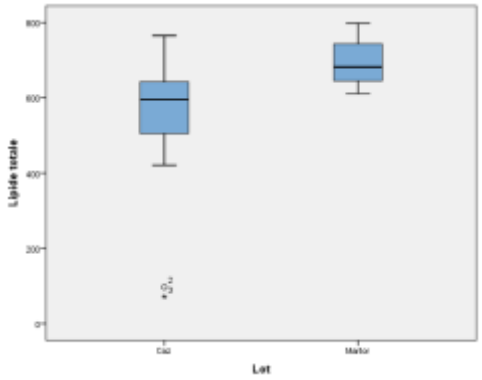

Figure 9. Distribution of the total lipids values

Normality was checked and Shapiro-Wilk test for statistically significant for the group of cases, we believe that the distribution is not normal values (Table 12).

Table 12. Testing normality of the distribution of values for total lipids

Normality tests

	Lot	Kolmogorov-Smirnov[a]			Shapiro-Wilk		
		Statistic	df	Sig.	Statistic	df	Sig.
Total lipids	Case	.218	15	.053	.811	15	.005
	Witness	.135	30	.175	.945	30	.124

a. Lilliefors Significance Correction

The null hypothesis from which we started in the statistical analysis performed using nonparametric Mann-Whitney test states that there are not significant differences between the values of total lipids recorded in the two groups in this study. (Table 13).

Table 13. Mann-Whitney Test of the Total lipids

Test Statistics[a]

	Total lipids
Mann-Whitney U	68.000
Wilcoxon W	188.000
Z	-3.781
Asymp. Sig. (2-tailed)	.000

a. Grouping Variable: Lot

Direct Bilirubin. Direct bilirubin was increased to a total of 13 patients with esophageal atresia. (Table 14).

Table 14. Descriptive analysis of the direct bilirubin

Descriptive analysis
Direct bilirubin

Lot	N	Mean	Std. Deviation	Minimum	Maximum	Median
Case	15	2.7793	3.15294	.16	9.46	1.3900
Witness	30	.1763	.05762	.05	.28	.1900
Total	45	1.0440	2.16914	.05	9.46	.2200

In the figure 10 is plotted descriptive characteristics of direct bilirubin.

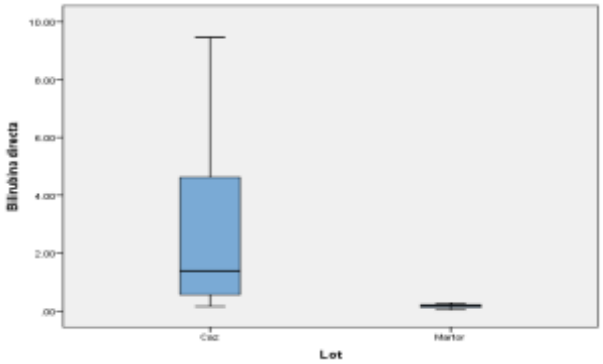

Figure 10. Distribution of the direct bilirubin values

Shapiro-Wilk test is statistically significant for the group of cases. (Table 15).

Table 15. Direct bilirubin testing distribution

Normality tests

	Lot	Kolmogorov-Smirnov[a]			Shapiro-Wilk		
		Statistic	df	Sig.	Statistic	df	Sig.
Direct bilirubin	Case	.296	15	.001	.759	15	.001
	Witness	.160	30	.047	.961	30	.323

a. Lilliefors Significance Correction

Mann-Whitney test is statistically significant ($p < 0.001$), so the null hypothesis is rejected and alternative hypothesis is accepted (alternative hypothesis argues that there are significant differences between the two groups) (Table 16).

Tabel 16. Mann-Whitney Test of the direct bilirubin

Test Statistics[a]

	Direct bilirubin
Mann-Whitney U	18.000
Wilcoxon W	483.000
Z	-4.991
Asymp. Sig. (2-tailed)	.000

a. Grouping Variable: Lot

Total bilirubin. Total bilirubin was increased to a total of 13 patients with esophageal atresia (Table 17).

Table 17. Descriptive analysis for the total bilirubin values

Descriptive analysis

Total bilirubin

Lot	N	Mean	Std. Deviation	Minimum	Maximum	Median
Case	15	7.7340	4.73660	1.16	16.89	6.9000
Witness	30	.6833	.18267	.43	1.18	.6100
Total	45	3.0336	4.29636	.43	16.89	.8500

Distribution of the total bilirubin values is shown compared in Figure 11.

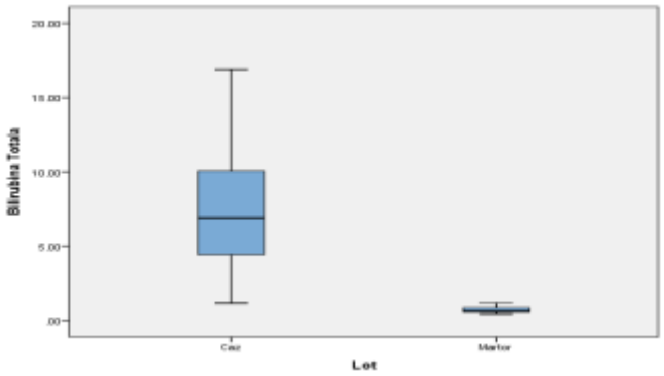

Figure 11. Distribution of the total bilirubin values

The control group presented values lie in a range between 0.43 mg/dl and 1.18 mg/dl, while for neonates with esophageal atresia values ranged from 1.16 mg/dl and a the maximum of 16.89 mg/dl. Tests to verify the normality result that of total bilirubin distribution is not a normal (Table 18).

Table 18. Analysis of normality distribution of the total bilirubin values

Normality tests

	Lot	Kolmogorov-Smirnov[a]			Shapiro-Wilk		
		Statistic	df	Sig.	Statistic	df	Sig.
Total bilirubin	Case	.219	15	.050	.924	15	.223
	Witness	.215	30	.001	.891	30	.005

a. Lilliefors Significance Correction

Mann-Whitney U test is highly statistically significant ($p < 0.001$), so the values seen in the lot of cases differ significantly from the values observed in the control group (Table 19).

Table 19. Mann Whitney test for total bilirubin

Test Statistics[a]

	Total Bilirubin
Mann-Whitney U	1.000
Wilcoxon W	466.000
Z	-5.396
Asymp. Sig. (2-tailed)	.000

a. Grouping Variable: Lot

Urea. The cases analized in the study show a mean urea value of 47.52 mg/dl (standard deviation is 21,188 mg/dl). Witnesses have an average value of 27.43 mg/dl (standard deviation of 10,136 mg/ dl). It notes that if newborns in the control group averages meet lower compared to the group of cases (Table 20).

Table 20. Descriptive analysis of the urea

Descriptive analysis

Urea

Lot	N	Mean	Std. Deviation	Minimum	Maximum	Median
Case	15	47.52	21.188	20	94	39.00
Witness	30	27.43	10.136	14	45	23.50
Total	45	34.13	17.386	14	94	33.00

Normal distribution of values is refuted by tests of normality, so to determine the statistical signifi-cance of the differences observed be used nonparametric tests (Table 21).

Table 21. Test for normality distribution of the urea

Normality tests

	Lot	Kolmogorov-Smirnov[a]			Shapiro-Wilk		
		Statistic	df	Sig.	Statistic	df	Sig.
Urea	Case	.195	15	.128	.907	15	.121
	Witness	.204	30	.003	.895	30	.006

a. Lilliefors Significance Correction

Mann-Whitney test is highly statistically significant (p = 0.001 and we can say that the two groups are statistically significant difference (Table 22).

Table 22. Mann-Whitney test for the urea

Test Statistics[a]

	Urea
Mann-Whitney U	90.000
Wilcoxon W	555.000
Z	-3.253
Asymp. Sig. (2-tailed)	.001

a. Grouping Variable: Lot

In conclusion urea present values significantly higher in neonates with esophageal atresia. From the group of cases, of the 15 patients with esophageal atresia 5 had elevated values of the blood urea.

Serum aminotransferases

TGP (Glutamatpiruvat-transaminase). Maximum recorded for TGP is 109 IU,

group registered newborns with esophageal atresia. Mean TGP for them is 41.93 UI (stan-dard deviation 24.849).

The average is higher than the infants in the control group where the mean is 24.50 IU (8831 IU standard deviation), 5 patients in the group of cases showing higher values of TGP's (Table 23).

Table 23. Descriptive analysis of the TGP

Descriptive analysis

TGP

Lot	N	Mean	Std. Deviation	Minimum	Maximum	Median
Case	15	41.93	24.849	8	109	47.00
Witness	30	24.50	8.831	12	39	21.00
Total	45	30.31	17.803	8	109	28.00

TGP values do not follow a normal distribution, then the t-test can not be used for objective statistical significance of the differences observed (Table 24).

Table 24. Tested for normality distribution of the TGP values

Normality tests

	Lot	Kolmogorov-Smirnov[a]			Shapiro-Wilk		
		Statistic	df	Sig.	Statistic	df	Sig.
TGP	Case	.205	15	.088	.893	15	.075
	Witness	.187	30	.009	.910	30	.015

a. Lilliefors Significance Correction

To test the statistical significance of differences between the two groups we used the Mann-Whitney test. This is statistically significant (p=0.01) so the differences observed between the two groups are not random (Table 25).

Table 25. Mann-Whitney test of the TGP

Test Statistics[a]

	TGP
Mann-Whitney U	118.500
Wilcoxon W	583.500
Z	-2.567
Asymp. Sig. (2-tailed)	.010

a. Grouping Variable: Lot

Serum calcium. The highest value is 11 mg/dl (batch control), and the lowest 5.20 mg/dl (at lot of cases) (Table 26).

Table 26. Descriptive analysis of the serum calcium

Descriptive analysis

Serum calcium

Lot	N	Mean	Std. Deviation	Minimum	Maximum	Median
Case	15	8.2533	1.26709	5.20	10.20	8.0000
Witness	30	9.8300	.51805	9.00	11.00	9.8000
Total	45	9.3044	1.11924	5.20	11.00	9.6000

In the cases studied, 11 patients had hypocalcemia, 10 of whom were premature. Other descriptive characteristics of the two groups, and the distribution of values can be seen in Figure 12.

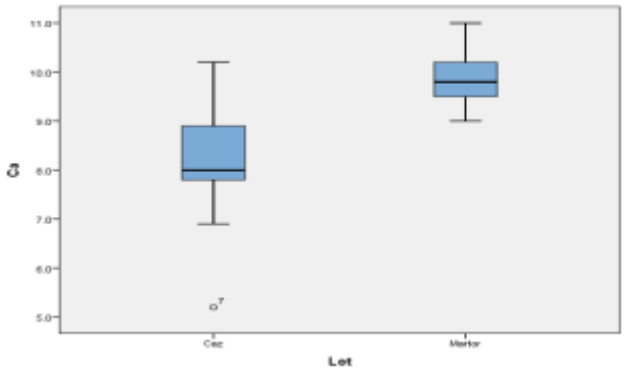

Figure 12. Distribution of the serum calcium values

Tests for normality were significant results for both groups (Table 27).

Table 27. Tested to determine the normality of calcium distributions

Normality tests

	Lot	Kolmogorov-Smirnov[a]			Shapiro-Wilk		
		Statistic	df	Sig.	Statistic	df	Sig.
Serum calcium	Case	.160	15	.200*	.947	15	.476
	Witness	.090	30	.200*	.973	30	.614

*. This is a Limita inferioară bound of the true significance.

a. Lilliefors Significance Correction

Because serum calcium levels follow a normal distribution, the comparison can be used with great fidelity test t. Test is statistically significant (Table 28).

Table 28. t Ttest for the serum calcium

t Test for independent samples

			Serum calcium	
			Homogeneous variances	Heterogeneous variances
Levene test for homogeneity of variances	F		10.796	
	Sig.		.002	
t Test	t		-5.943	-4.630
	df		43	16.383
	Sig. (2-tailed)		.000	.000
	The mean difference		-1.57667	-1.57667
	The standard error of the difference		.26528	.34056
	95% Confidence interval of the difference	Lower limit	-2.11165	-2.29725
		Upper limit	-1.04168	-.85608

Sodium. Regarding sodium levels observed in the control group there higher value than normal, up to maximum of 233 mmol/L. Mean concentration value of sodium ions for infants in the control group is 148.28 mmol/l (standard deviation 21.595 mmol/l). For cases there is a lower mean values, a mean of 127 mmol/l (standard deviation of 11,225 mmol/l), the minimum value of 106 mmol/l and the maximum value of 142 mmol/l (Table 29).

Tabel 29.. Descriptive analysis of the serum sodium values

Descriptive analysis
Sodium

Lot	N	Mean	Std. Deviation	Minimum	Maximum	Median
Case	15	127.00	11.225	106	142	129.00
Witness	30	148.28	21.595	135	233	141.00
Total	45	141.19	21.223	106	233	139.00

The box-plot in figure 13 is plotted how they are distributed serum sodium values compared for the two groups. If there are multiple witnesses who are considered outlier values.

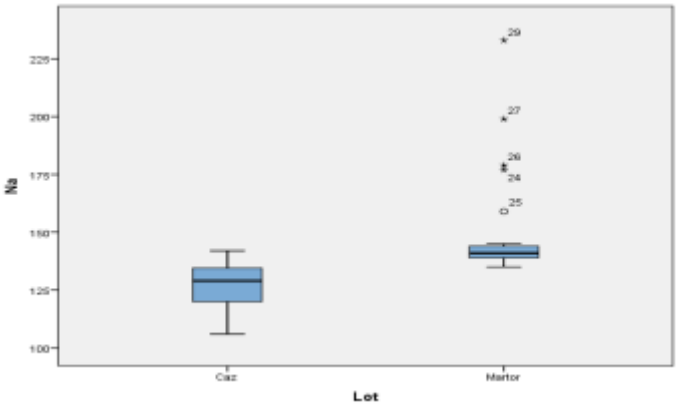

Figure 13. Distribution of the serum sodium values

For infants in group cases the distribution did not differ significantly from a normal distribution (according to the test Shapiro-Wilk) (Table 30).

Table 30. Tested for the normality distribution of the serum sodium values

Normality tests

	Lot	Kolmogorov-Smirnov[a]			Shapiro-Wilk		
		Statistic	df	Sig.	Statistic	df	Sig.
Natremia	Case	.237	15	.023	.926	15	.235
	Witness	.394	30	.000	.567	30	.000

a. Lilliefors Significance Correction

Nonparametric Mann-Whitney test shows a high statistical significance ($p < 0.001$) (Table 31).

Table 31. Mann-Whitney test for the serum sodium levels

Test Statistics[a]

	Sodium
Mann-Whitney U	43.500
Wilcoxon W	163.500
Z	-4.379
Asymp. Sig. (2-tailed)	.000

a. Grouping Variable: Lot

CBC (complet blood cell). A complete blood count is a basic screening test one of the most frequently required laboratory tests often are the first step in establishing the diagnosis of haematological status of various hematologic and non-hematologic disorders (Synevo Laboratory, 2010).

Leukocytes. Both the minimum and maximum value occurred in group cases WBC ranged between 3,900/mm^3 and 18,600/mm^3. For lot of witnesses values were in the range 5700-9800/mm^3. For this cases, 2 patients were present elevated leukocyte count (Table 32).

Table 32. Descriptive analysis of the leukocyte

Descriptive analysis

Leukocyte

Lot	N	Mean	Std. Deviation	Minimum	Maximum	Median
Case	15	7844.67	3407.691	3900	18600	7850.00
Witness	30	7710.00	1185.211	5700	9800	7550.00
Total	45	7754.89	2150.535	3900	18600	7600.00

From the box-plot shown in figure 14 identifies a case with elevated total white blood cell, respectively 18600/mm^3 an outlier that differ greatly from the values seen in this cases the remaining values are lower than the maximum considered normal.

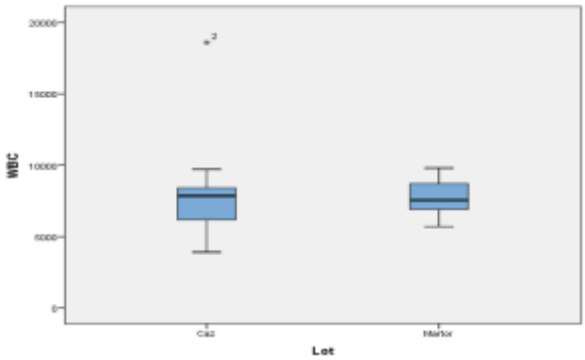

Figure 14. Distribution of the leukocytes values

We tested if the distribution of WBC values is significantly different or not from a normal distribution. Becouse Shapiro-Wilk test is statistically significantly for the group of cases, we conclude that in this case a gaussian distribution is not observed (Table 33).

Table 33. Tested for the normal distribution of the leukocytes values

Normality tests

	Lot	Kolmogorov-Smirnov[a]			Shapiro-Wilk		
		Statistic	df	Sig.	Statistic	df	Sig.
Leukocytes	Case	.290	15	.001	.754	15	.001
	Witness	.070	30	.200*	.967	30	.454

*. This is a Limita inferioară bound of the true significance.

a. Lilliefors Significance Correction

Due to the fact that the values do not follow a normal distribution, it is necessary to use nonparametric compared tests. Using the Mann-Whitney test calculated value for p is 0.621, well above the limit of statistical significance of 0.05, so there are not significant differences in the number of leukocytes between the two groups studied (Table 34).

Table 34. Mann-Whitney test for the leukocytes

Test Statistics[a]

	Leukocytes
Mann-Whitney U	204.500
Wilcoxon W	324.500
Z	-.494
Asymp. Sig. (2-tailed)	.621

a. Grouping Variable: Lot

Erythrocytes. Neonates with esophageal atresia were reported 4 cases in which the number of red blood cells was lower due to anemia secondary after aspiration broncho-pneumonia, infectious complication associated esophageal atresia (Table 35).

Table 35. Descriptive analysis for the erythrocyte

Descriptive analysis
Erythrocyte

Lot	N	Mean	Std. Deviation	Minimum	Maximum	Median
Case	15	4.5993	.93337	2.90	5.90	4.7000
Witness	30	5.5527	.64461	4.50	6.90	5.5750
Total	45	5.2349	.87041	2.90	6.90	5.4000

Descriptive characteristics of the two groups are shown graphic in box-plot of figure 15.

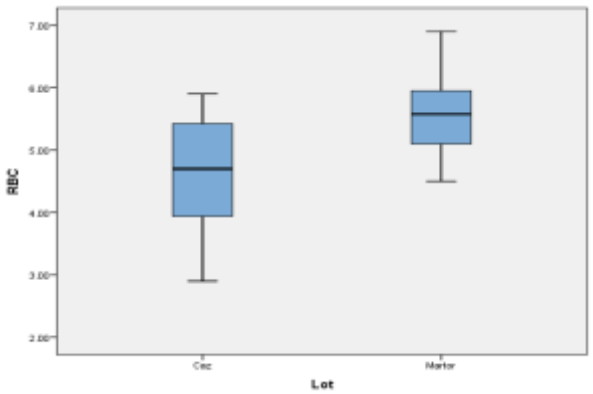

Figure 15. Distributions of the erythrocytes values

We test the degree of normality of the distribution the number erythrocytes values. As the statistical significance is not touched (level 0.05), it can be observed that the values follow a normal distribution (Table 36).

Table 36. Tests for the normal distribution of the erythrocyte values

Normality tests

	Lot	Kolmogorov-Smirnov[a]			Shapiro-Wilk		
		Statistic	df	Sig.	Statistic	df	Sig.
Erythrocytes	Case	.138	15	.200*	.947	15	.478
	Witness	.111	30	.200*	.958	30	.270

*. This is a Limita inferioară bound of the true significance.

a. Lilliefors Significance Correction

Levene test is not statistically significant (p=0.068), so the variances did not differ statistically significant. In conclusion, we used the t test assuming equal variances (Table 37).

Table 37. t Test for erythrocyte

t Test for independent samples

			Erythrocyte	
			Homogeneous variances	Heterogeneous variances
Levene test for homogeneity of variances	F		3.498	
	Sig.		.068	
t Test	t		-4.015	-3.555
	df		43	20.900
	Sig. (2-tailed)		.000	.002
	The mean difference		-.95333	-.95333
	The standard error of the difference		.23746	.26820
	95% Confidence interval of the difference	Lower limit	-1.43222	-1.51124
		Upper limit	-.47445	-.39543

The calculated value for t is 4.015 ("-" sign indicates the direction of the difference), which for 43 degrees of freedom corresponds to $p<0.001$. So there is statistically significant difference between the two groups, the average being 0.95 x 106/mm^3 (CI95% 0.474 to 1.432 x106/mm^3), witnesses present a higher average number of erythrocytes. The effect is of great clinical importance, d = 1.3 (95% CI 1.07 to 1.77).

Hemoglobin. Mean hemoglobin (Hb) for the group of cases is 14.027 g/dL with a standard deviation of 3.1 g/dl. The values are in the range of 10 to 21.2 g/dl, so the values are both greater and smaller than normal. In this cases the 6 patients had anemia with hemoglobin levels below the lower limit of normal (Table 38).

Table 38. Descriptive analysis for the hemoglobin

Descriptive analysis

Hemoglobin

Lot	N	Mean	Std. Deviation	Minimum	Maximum	Median
Case	15	14.027	3.1040	10.0	21.2	13.500
Witness	30	15.050	.4232	14.2	15.8	15.050
Total	45	14.709	1.8498	10.0	21.2	15.000

The control group includes hemoglobin values ranging from 14.2 to 15.8 g/dl. The mean of the hemoglobin is 15.05 g/dl. The box-plot in figure 16 plot the characteristics of the two groups point of view of hemoglobin.

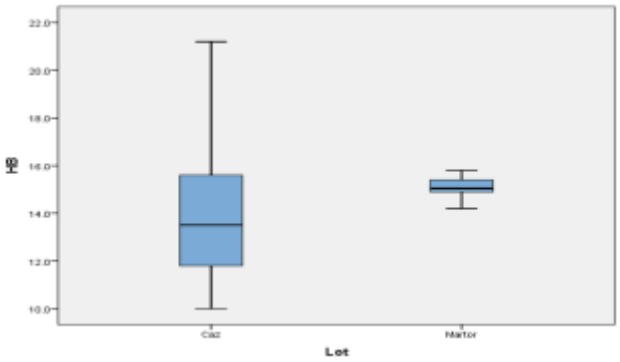

Figure 16. Distribution of the hemoglobin values

The normality was tested using the Shapiro-Wilk test. The result is not statistically significant for both groups (Table 39).

Table 39. Tested for the normal distribution of the hemoglobin

Normality tests

	Lot	Kolmogorov-Smirnov[a]			Shapiro-Wilk		
		Statistic	df	Sig.	Statistic	df	Sig.
Hemoglobin	Case	.167	15	.200*	.937	15	.341
	Witness	.128	30	.200*	.948	30	.151

*. This is a Limita inferioară bound of the true significance.

a. Lilliefors Significance Correction

Since the observed values of hemoglobin in neonates in this study comply with normal distribution, for determining the level of mean difference and its statistical significance we used the t test. Since $p<0.001$, will be used t-test for unequal variances (Table 40).

Table 40. t Test for the hemoglobin

t Test for independent samples

			Hemoglobin	
			Homogeneous variances	Heterogeneous variances
Levene test for homogeneity of variances	F		44.812	
	Sig.		.000	
t Test	t		-1.793	-1.271
	df		43	14.261
	Sig. (2-tailed)		.080	.224
	The mean difference		-1.0233	-1.0233
	The standard error of the difference		.5708	.8052
	95% Confidence interval of the difference	Lower limit	-2.1744	-2.7473
		Upper limit	.1277	.7006

T calculated is set -1271 ("-" sign indicates the direction of the gap - in this case the fact that the mean hemoglobin value for the lot of cases is lower than the control group).

Platelets. In the group with esophageal atresia that we have studied a number of 3 patients had low total number of platelets below the lower limit of normal. Hemorrhagic syndrome externalizes when thrombocytopenia is generally less than 60.000/mm ^{3} (Lupea, 2000) (Table 41).

Table 41. Descriptive analysis of the platelets values

Descriptive analysis
Platelets

Lot	N	Mean	Std. Deviation	Minimum	Maximum	Median
Case	15	198466.67	65825.382	80000	299000	176000.00
Witness	30	226700.00	32303.678	189000	289000	224500.00
Total	45	217288.89	47409.062	80000	299000	212000.00

Neonates in the control group in the study values were in the range of 189,000/mm ^{3} - 289,000/mm ^{3}, the average values being 224,500.00/mm ^{3}. Graphic characteristics of the two groups are shown in box-plot in figure 17.

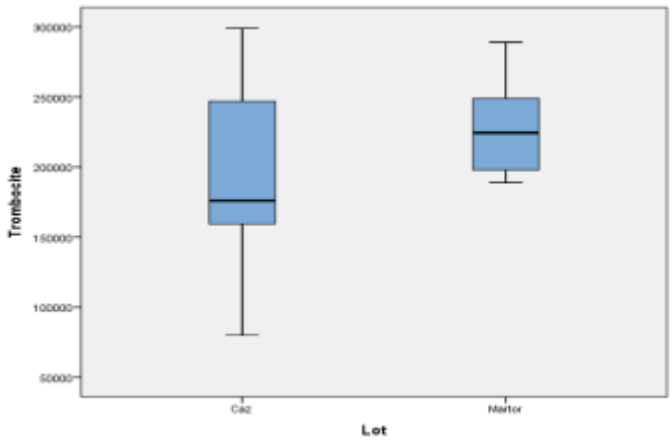

Figure 17. Distribution values of platelet count

Shapiro-Wilk test is statistically significant for lot of witnesses group, so that in order to determine the statistical significance of observed differences require the use of a non-parametric test (Table 42).

Table 42. Testing normality distribution of the platelets

Normality tests

	Lot	Kolmogorov-Smirnov[a]			Shapiro-Wilk		
		Statistic	d	Sig.	Statistic	df	Sig.
Platelets	Case	.167	15	.200*	.956	15	.626
	Witness	.168	30	.030	.892	30	.005

*. This is a Limita inferioară bound of the true significance.

a. Lilliefors Significance Correction

Mann-Whitney U test is not statistically significant (p=0.101), so the differences observed between the two groups occurred due to the hazard (Table 43).

Table 43. Mann-Whitney test for the number of the platelets

Test Statistics[a]

	Platelets
Mann-Whitney U	157.000
Wilcoxon W	277.000
Z	-1.638
Asymp. Sig. (2-tailed)	.101

a. Grouping Variable: Lot

Serum iron. In the cases studied the mean value of serum iron was 70.47 mg/dl with a standard deviation of 29.636 mg/dl. The minimum value is 39 mg/dl, and the value of the maximum amount is 132 mg/ dl. In this cases 4 patients with esophageal atresia had lower values of serum iron (Table 44).

Table 44. Descriptive analysis of the serum iron values

Descriptive analysis

Serum iron

Lot	N	Mean	Std. Deviation	Minimum	Maximum	Median
Case	15	70.47	29.636	39	132	57.00
Witness	30	97.17	21.670	60	134	97.50
Total	45	88.27	27.404	39	134	89.00

In the Box-plot of figure 18 is Graphic various descriptive characteristics of the two groups.

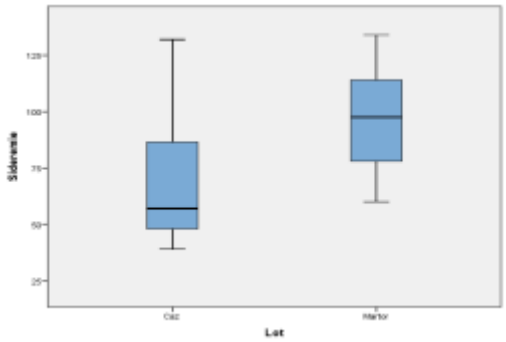

Figure 18. Distribution of the serum iron values

Tests for normality of distribution values are not statistically significant so the null hypothesis that the observed distribution does not differ significantly from a normal distribution can not be rejected (Table 45).

Table 45. Tests for determination normality distribution of the serum iron values

Normality tests

		Kolmogorov-Smirnov[a]			Shapiro-Wilk		
	Lot	Statistic	df	Sig.	Statistic	df	Sig.
Serum iron	Case	.209	15	.078	.884	15	.055
	Witness	.125	30	.200*	.952	30	.187

*. This is a Limita inferioară bound of the true significance.

a. Lilliefors Significance Correction

Levene test for equality of variance is not statistically significant, so the statistical analysis t test was used for equal variances (Table 46).

Table 46. t Test for the serum iron

t Test for independent samples

			Serum iron	
			Homogeneous variances	Heterogeneous variances
Levene test for homogeneity of variances	F		2.204	
	Sig.		145	
t Test	t		-3.439	-3.100
	df		43	21.736
	Sig. (2-tailed)		.001	.005
	The mean difference		-26.700	-26.700
	The standard error of the difference		7.763	8.614
	95% Confidence interval of the difference	Lower limit	-42.356	-44.577
		Upper limit	-11.044	-8.823

The average difference between the mean values of serum iron in the two groups studied is 26.70 mg/ dl group of newborns with esophageal atresia showing lower values of serum iron, the difference being statistically significant (p=0.001).

The effect size is calculated using the Cohen coefficient, the statistic has a value of 1.11 (95% IC -6.64 to 16.11). One can thus say that the effect on serum iron esophageal atresia is a big one.

Correlation between main biochemical markers detected in neonates with esophageal atresia

In order to determine the existence of possible correlations between several different markers addressed in this study we chose the statistical test applied to the scores of the sample Spearman(rho) rank correlation coefficient.

In order to determine the existence of possible correlations between albumin and serum calcium we chose the sample correlation coefficient nonparametric statistical test of their rank Spearman (rho). It shows a value of 0.770 at $p<0.05$. These values would indicate a positive significant correlation between albumin and serum calcium (Table 47).

Table 47. The correlation between Albumin and Serum calcium

Correlations

			Albumin	Serum calcium
Spearman's rho	Albumin	Correlation Coefficient	1.000	.770**
		Sig. (2-tailed)	.	.001
		N	15	15
	Serum calcium	Correlation Coefficient	.770**	1.000
		Sig. (2-tailed)	.001	.
		N	15	15

**. Correlation is significant at the 0.01 level (2-tailed).

After the preparation the graph "cloud of points" can see that therea correlation quite close to the linear one (Figure 19).

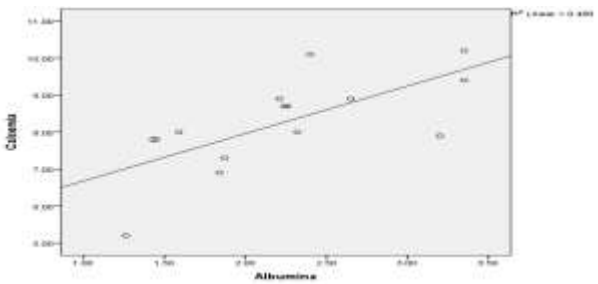

Figure 19. Graph cloud of points for Serum calcium – Albumin

To investigate possible links between cholesterol metabolism and serum total protein sample we applied the Spearman(rho) rank correlation coefficient. The result is a value of the Spearman (rho) coefficient of 0.651 at $p<0.01$, being statistically significant (Table 48).

Table 48. The correlation between total protein and serum cholesterol

Correlations

			Total Protein	Serum Cholesterol
Spearman's rho	Total Protein	Correlation Coefficient	1.000	.651**
		Sig. (2-tailed)	.	.009
		N	15	15
	Serum Cholesterol	Correlation Coefficient	.651**	1.000
		Sig. (2-tailed)	.009	.
		N	15	15

**. Correlation is significant at the 0.01 level (2-tailed).

Upon completion schedule "cloud of points" shows that the group of cases 5 patients the presence of low serum cholesterol and 14 cases had hypoproteinemia (Figure 20).

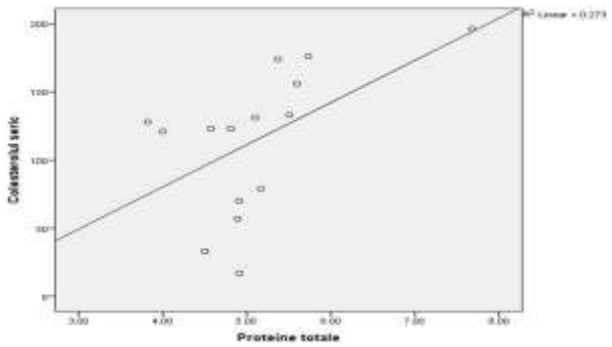

Figure 20. Graph cloud of points for serum Cholesterol - Total protein

In order to investigate the existence of possible links between glucose and the protidic metabolism there were determined the blood glucose and globulins values and chose the statistical test applied to the scores for the group analyzed the sample Spearman(rho) rank correlation coefficient. The result was a value of Spear-man(rho) coefficient of 0.690 at $p<0.01$ which indicating a statistically significant correlation. (Table 49).

Table 49. The correlation between Blood glucose and Globulin

Correlations

			Blood glucose	Globulin
Spearman's rho	Blood glucose	Correlation Coefficient	1.000	.690**
		Sig. (2-tailed)	.	.004
		N	15	15
	Globulin	Correlation Coefficient	.690**	1.000
		Sig. (2-tailed)	.004	.
		N	15	15

**. Correlation is significant at the 0.01 level (2-tailed).

The chart "cloud of points" shows that in this case the positive correlation exists between the values of the two markers does not have a linear character (Figure 21).

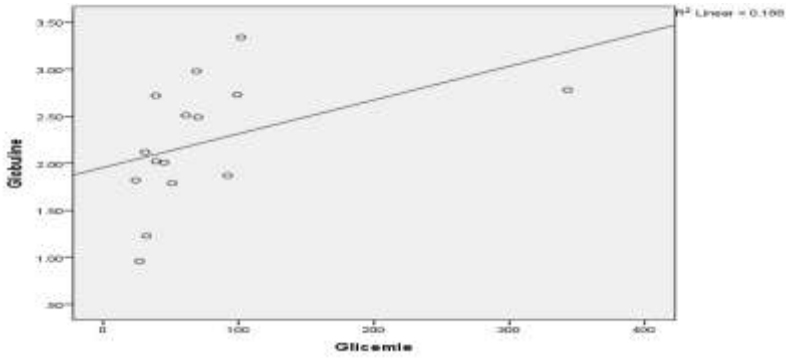

Figure 21. Graph cloud of points Globulin – Blood Glucose

Calculating the Spearman(rho) correlation coefficient for globulins and serum calcium shows a value of 0.724 at <0.01, which shows a statistically significant correlation (Table 50).

Table 50. The correlation between Globulin and Serum calcium

Correlations

			Globulin	Serum calcium
Spearman's rho	Globuline	Correlation Coefficient	1.000	.724**
		Sig. (2-tailed)	.	.002
		N	15	15
	Serum calcium	Correlation Coefficient	.724**	1.000
		Sig. (2-tailed)	.002	.
		N	15	15

**. Correlation is significant at the 0.01 level (2-tailed).

The chart "cloud of points" shows a correlation closer to a linear one (Figure 22).

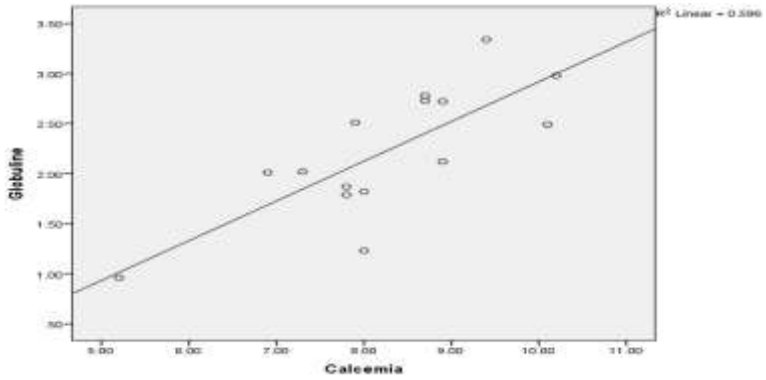

Figure 22. Graph cloud of points Globulune - Serum calcium

In order to investigate the possibility of possible links between direct bilirubin and uric acid me-tabolism there were determined the values of the two markers analyzed. In the case of direct bilirubin and uric acid obtained Spearman(rho) coefficient of -0.588 at $p<0.05$. The value of the correlation coefficient obtained in this caseis relatively small and indicating the presence of weak negative correlations between the two quite thin markers (Table 51).

Table 51. The correlation between uric acid and direct bilirubin

Correlations

			Uric Acid	Direct Bilirubin
Spearman's rho	Uric Acid	Correlation Coefficient	1.000	-.588*
		Sig. (2-tailed)	.	.021
		N	15	15
	Direct Bilirubin	Correlation Coefficient	-.588*	1.000
		Sig. (2-tailed)	021	.
		N	15	15

*. Correlation is significant at the 0.05 level (2-tailed).

The chart "cloud of points" actually shows that the correlation is far from a linear one (Figure 23).

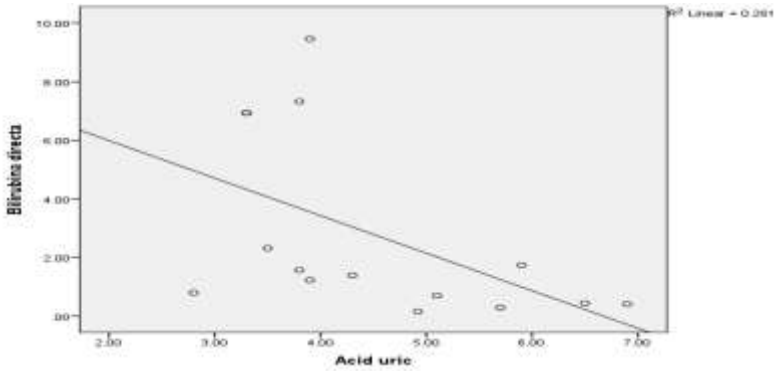

Figure 23. Graph cloud of points Direct Bilirubin - Uric Acid

In order to investigate the possibility of possible links between potassium and direct bilirubin metabolism we determined serum potassium and direct bilirubin levels and then applied the scores obtained for the sample group analyzed the Spearman(rho) rank correlation coefficient. The result was a value of Spearman(rho) coefficient of 0.690 to $p<0.01$ (Table 52).

Table 52. The correlation between Serum Potassium and Direct Bilirubin

Correlations

			Serum Potassium	Direct Bilirubin
Spearman's rho	Serum Potassium	Correlation Coefficient	1.000	.650**
		Sig. (2-tailed)		.009
		N	15	15
	Direct Bilirubin	Correlation Coefficient	.650**	1.000
		Sig. (2-tailed)	.009	.
		N	15	15

**. Correlation is significant at the 0.01 level (2-tailed).

The chart "cloud of points" shows that the group of cases varies between serum potassium 2.9 mmol/l the lowest value and 8.65 mmol/l which is the highest value recorded, and direct bilirubin was increased to a total of 13 patients with esophageal atresia, maximum recorded value was 9.46 mg/dl.

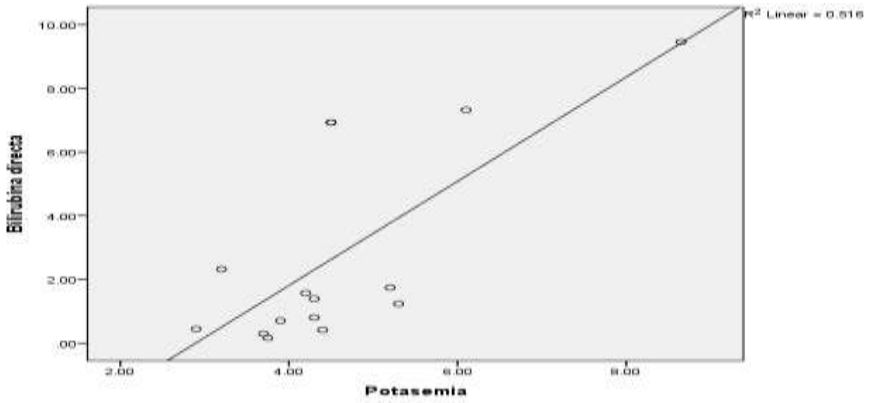

Figure 24. Graph cloud of points Direct Bilirubin – Potassium

One can also observe in the graph that in this case it seems to be little correlation close to one linear than other correlations analyzed in this section (Figure 24).

CONCLUSIONS AND RECOMMENDATIONS

1. Antenatal diagnosis of esophageal atresia often difficult to realise it is based on the presence of the following elements: hydramnios, prematurity and ultrasound the absence or low volume of gastric pouch on atresia of type II and dilatation upper esophageal sac.

2. Postnatal diagnosis of oesophageal atresia is based on the following elements: radiologic

examination probe radio-opaque, thoraco-abdominal radiographs, and performing the balance associated malformations.

3. Blood glucose. The patients with esophageal atresia had mean blood glucose values of 74.93 mg/dl lower compared to the control group where the mean value was 90.63 mg/dl. In the cases of all studied 15 patients with esophageal atresia, 6 patients blood glucose was low.

4. Hypoproteinemia occur through: low intake of protein and excess protein cabolism. Of the total number of cases studied, 14 cases had lower values of protein levels.

5. Total lipids. The minimum amount was 72 mg/dl well below the normal minimum level of 600 mg /dl, and the maximum value of 765 mg/dl, this being in the normal range. Of the 15 cases with esophageal atresia studied, a total of 7 patients newborns had low lipemia.

6. Hyperbilirubinemia is frequent in the presence of physiological jaundice. Direct bilitubin and total bilirubin a was increased to a total of 13 patients with a esophageal atresia.

7. Urea presents values statistically significant higher in neonates with esophageal atresia. From the group of cases, 15 patients with esophageal atresia 5 had increased levels of blood urea.

8. TGP. Maximum recorded for TGP is 109 IU group registered newborns esophageal atresia, of which 5 patients had higher values of TGP's.

9. Electrolyte disorders are produced especially when there is an extracellular dehydration or risk thereof in the event of non-set by oral intake.

a) Serum calcium. In the cases studied, 11 patients had hypocalcemia, 10 of whom were premature, and 7 of premature presented the various associated malformations (cardiac, ano-rectal).

10. Complete blood count test (CBC)

a) Leukocytes. For cases in the study group, two patients had increased levels of blood leukocytes.

b) The number of erythrocytes presents mean value lower in neonates with esophageal atresia. At the newborns with esophageal atresia there were reported 4 cases in which the number of red blood cells was lower.

c) Hemoglobin (Hb). Of the lot of cases six patients had anemia with hemoglobin levels below the lower limit of normal, as they were premature.

d) With regard to the total number of platelets in the group with esophageal atresia that we have studied a total of 3 patients had low total number of platelets, below the lower limit of normal.

e) Serum iron. The minimum value is 39 mg/dl, and the value of the maximum amount is 132 mg/ dl. In this cases 4 patients with esophageal atresia had lower values of serum iron

11. Correlations between the main biochemical markers detected in neonates with esophageal atresia.

a) To determine the existence of possible correlations between albumin and serum calcium, we have chosen a statistical test applied to the scores for the group analyzed the sample correlation coefficient non-parametric Spearman(rho) rank. It shows a value of 0.770 at $p<0.05$. These values would indicate a positive significant correlation between albumin and serum calcium.

b) In order to investigate possible links between serum cholesterol metabolism and serum total protein applied the sample correlation coefficient Spearman(rho)

rank in the case of the 2 markers analyzed. The result was a value of Spearman(rho) coefficient of 0.651 at $p< 0.01$. Following the completion schedule "cloud of points" shows that the group of cases 5 patients had low serum cholesterol and 14 cases had hypoproteinemia .

c) In order to investigate the possibility of possible links between glucose metabolism and the protidic there were determined the blood glucose and the globulins and applying the sample correlation coefficient of Spearman(rho) rank resulted a value of 0.690 at $p< 0.01$. After drawing the graph "cloud of points" can be seen in lot of cases that 10 patients had low levels of globulin, and in 6 patients blood sugar was low.

d) In order to investigate the possibility of links between calcium and the protidic metabolism there were determined calcium and globulins level values. Calculating the Spearman(rho) correlation coefficient for globulins and serum calcium shows a value of 0.724 at $p<0.01$, indicating a statistically significant correlation. In this case, it can be seen from the graph "cloud of points" a correlation closer to a linear one.

e) In order to investigate possible links between the direct bilirubin and uric acid metabolism there were determined the values of the two markers analyzed. In the case of direct bilirubin and uric acid we obtained a Spearman(rho) coefficient of -0.588 at $p<0.05$. The value of the correlation coefficient obtained in this case is a relatively small negative correlation indicates the presence of rather weak between the two markers.

f) In order to investigate the possibility of possible links between potassium and direct bilirubin metabolism we determined serum potassium and direct bilirubin levels and applied scores obtained for the analized group of correlation coefficient Spearman(rho) rank.

The result was a value of Spearman rho) coefficient of 0.690 at $p< 0.01$. The chart "cloud of points" shows that in this case the correlation seems to be something closer to a linear one.

12. The purpose of this paper is to emphasize that a correct diagnosis and early performed immediately after birth, followed by metabolic imbalances (correction hipoproteinemiilor, hypoglycemia, lipid lowering) of electrolyte and acid-base imbalances, correcting hypoxia and establishment of specialized surgical treatment cases with good prognosis ensure patient survival with a normal life later.

13. Index esophageal atresia healing is 80-90% in western countries. For the neonatology department of Clinical Emergency Hospital "St. Andrew" Constanţa the healing index of the esophagus atresia is 60% because of the total 15 infants

with the esophageal atresia in the study, 9 patients were cured and were released which represents a percentage of 60% and 6 patients were died during admission that represents a percentage of 40%. If in the cases with poor prognosis the treatment is difficult, requiring complex therapeutic means, the cases with favorable prognosis should heal without sequelae. Hence the need for early diagnosis before installing the lung lesions. This diagnosis it is possible in our country in the maternity, immediately after childbirth.

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