Immunological Evaluation of Pediatric Patients with Congenital Heart Diseases

Prof. Dr. Hanan Abd-Allah El-Gamal
Professor of Pediatrics in Institute of Post-graduate Childhood Studies
Ain Shams University
Prof. Dr. Ayman Mansour Abd-Algoad
Professor of Pediatrics in
National Research center
Dr. Dina Ahmed Soliman
Lecture Of Clinical Pathology
Ain Shams University
Dr. Inas Refay El-Sayed EL-Alamy

Abstract:

Evaluation of some immunological functions among specially selected pediatric patients with congenital heart defects and history of recurrent unusual infections, and comparing them with reference values for normal healthy subjects of a matched age, sex, and culture.

Patients and methods:

Out of 300 patients with established congenital heart disease (CHD), we selected fifty pediatric patients (Group I) suffering from a history of recurrent unusual infections. They were surveyed for the immune profile. They were chosen from the clinics of Pediatric Cardiology Department, Cairo University within one year. Congenital cardiac defects were diagnosed by two -dimensional echocardiography. The studied patients were selected on conservative treatment and not submitted to definitive or palliative heart surgical correction. They were further subdivided into two subgroups; subgroup IA with cyanotic CHD; subgroup IB with acyanotic CHD. The exclusion criteria encompassed serious medical illness; variables affecting immune system as connective tissue diseases (rheumatic diseases), other congenital heart anomalies with cell mediated immune deficiency (Di-George syndrome); rheumatic heart diseases; e.g. corticosteroid therapy; a history of prematurity, intrauterine growth retardation, and neurologic disability as well as incapability for providing the necessary data. They were previously hospitalized with unusual recurrent infections; such as two or more systemic, or serious bacterial infections; three, or more serious respiratory or documented bacterial soft tissue infections as cellulitis, draining otitis media, or lymphadenitis within one year; infections with common childhood pathogens but of unusual severity. Immunological evaluation entailed quantitative estimation of serum levels of

immunoglobulins (IgG, IgA, IgM, and IgE) and complement (C_3, and C_4). The results were compared with reference values for normal healthy age and sex matched infants and children, serving as a control Group (Group II). Data were statistically analyzed using SPSS package software version 14.0©

Results:

Fifty children (age range 4-33 months) with established congenital heart disease (CHD) were surveyed for the immune profile (Group I). They were subdivided into 2 subgroups; 28 cases (56%) in subgroup IA with congenital cyanotic heart diseases with 14 males and 14 females (M: F= 1: 1), and 22 cases (44%) with congenital acyanotic heart diseases in subgroup IB, with 10 males and 12 females (M: F =1: 1.2). They were subjected for immunological evaluation. The mean levels of IgG, IgM, and IgE were significantly higher in subgroup IA as compared to either subgroup IB or the control Group. Serum C_3 levels were low in 22 cases (44%), and this may contribute to their increased susceptibility to infections. High serum levels of C_3 were noticed in 7 cases (14%), while higher serum levels of C_4 were noticed in 11 cases (22%). These findings are being suggestive of the presence of chronic infections.

Conclusion:

Immune dysfunction is prevalent amongst pediatric patients suffering from CHD, with unusual chronic recurrent infections. Early and accurate diagnosis is essential to ensure that optimal treatment is given and to minimize the risk of progressive or irreversible lung damage. There is a clear evidence of an association between malnutrition which is prevalent among such patients, and poor wound healing, impaired immunity, and an increased risk of postoperative pneumonia.

Introduction:

Congenital heart diseases (CHD) are common pediatric problems that exist primarily at birth. They are characterized by gross structural abnormalities of the heart or the great vessels that actually interfere with normal cardiac function[1].

Immunodeficiency in association with CHD was first recognized in Di-George syndrome[2]. Early recognition of cell-mediated immunodeficiency (CMID) may be vital to the survival of a newborn. The recognition of immunodeficiency is likely to help in the management of infections with prompt anti- microbial therapy.[3] Complement immunodeficiency accounts for about 18% of primary immunodeficiency. Deficiency of C_3 and C_5 result in severe recurrent bacterial infections, while deficiencies of late components (C_6, C_7, C_8) result in recurrent meningococcal infections[4]. Neutropenia is frequently observed in preterm infants and those with intrauterine growth retardation; it increases the risk for sepsis. Mortality is increased when sepsis is associated with severe sepsis-induced neutropenia and bone marrow depletion[5].

Evaluation of immune function should be initiated for children with clinical manifestations of a specific immune disorder or with unusual, chronic, or recurrent infections such as one or more systemic bacterial infections (sepsis, meningitis); two or more serious respiratory or documented bacterial infections (cellulitis, draining otitis media, pneumonia, or lymphadenitis) within 1 yr; serious infections occurring at unusual sites (liver,or brain abscess); infections with unusual pathogens (Aspergillus, Serratia marcescens, Nocardia, or Burkholderia cepacia); and infections with common childhood pathogens but of unusual severity[6].

Children with defects in antibody production, phagocytic cells, or complement proteins have recurrent infections with encapsulated bacteria, such

as Streptococcus pneumoniae, Haemophililus influenzae, and staphylococcus, and may grow and develop normally despite their recurring infections, unless they develop bronchiectasis from repeated lower respiratory tract bacterial infections or persistent enteroviral infections of the central nervous system[7].

Brain abscesses can occur in children on account of embolization due to congenital heart disease with right-to-left shunts (especially tetralogy of Fallot)[8].

Infective endocarditis is a serious potential fatal infection which principally occurs in children with pre-existing congenital heart disease. A predisposing factor as surgery, dental procedure or intravenous catheter is present in one third of cases.[9] Two organisms account for the majority of cases; Streptococcus viridians (50%) and staphylococcus aureus (30%). Other bacteria as Pseudomonas, Hemophilus influenza and Streptococcus pneumoniae may be occasionally responsible. Viruses or fungi (Candida) are rare causative agents[10].

Patients And Methods:

Out of 300 patients with established congenital heart disease (CHD), we selected fifty pediatric patients (Group I) suffering from a history of recurrent unusual infections. They were surveyed for the immune profile. They were chosen from the clinic of Pediatric Cardiology Department, Cairo University within one year, starting from October 2008 to September 2009. Congenital cardiac defects were diagnosed on the basis of two -dimensional echocardiography. The studied patients were selected on conservative treatment and not submitted to definitive or palliative heart surgical correction. They were further subdivided into two subgroups; subgroup IA (cyanotic); subgroup IB (acyanotic). They were previously hospitalized with unusual chronic recurrent infections; such as two or more systemic, or serious bacterial infections; three, or more serious respiratory or documented bacterial soft tissue infections as cellulitis, draining otitis media, or lymphadenitis within one year; infections with common childhood pathogens but of unusual severity. The exclusion criteria encompassed serious medical illness; variables affecting immune system as connective tissue diseases (rheumatic diseases) and other congenital heart anomalies with cell mediated immune deficiency (Di-George syndrome); rheumatic heart diseases; corticosteroids therapy; a history of prematurity, intrauterine growth retardation, neurologic disability as well as incapability for providing the necessary data. All studied patients were subjected to thorough history taking, including onset of cyanosis, hypercyanotic spells, tachypnea, feeding difficulty, poor weight gain, repeated chest infections, and congestive heart failure. Information on socioeconomic status, parental education status, birth weight and nutritional history, number of siblings, and the timing, quality, and quantity of nutrients ingested during weaning period and at the time of the study were obtained through careful interviews with parents. The studied patients were subjected to complete physical examination, checking their weight, length, head circumference, and physical signs of malnutrition, such as skin lesions, and thin and weak hair. Laboratory investigations entailed a complete blood picture, mainly differential white blood cell count, hemoglobin concentration, serum iron level, total iron binding capacity, and serum calcium studies. Karyotyping was performed for dysmorphic patients. Immunological evaluation for studied was done via quantitative estimation of serum immunoglobulins and complement levels. A nephelometer (Minineph) analyzer was used for assaying serum levels of IgG, IgA, IgM, C_3, and C_4.

Serum IgE level was measured using ELISA technique. Blood samples were collected in the morning after an overnight fast. About 2cc were allowed to collect naturally by venipuncture and the serum was separated as soon as possible to prevent hemolysis. Sera were stored aliquoted and freezed at -70 C or below. Sample dilutions were freshly prepared on the day of assay. As with all good laboratory practice, controls were run with every patch of the samples. The results were compared with reference values for normal healthy age, and sex matched subjects, serving SPSS package software version 14.0©, taking the 5% level as the level of significance. The local ethical committee approved the study protocol. Informed consents were obtained from the parents of the subjects.

Table (1) Normal Serum Immunoglobulin Values in Children

Age	IgG g/L	LgA g/L	LgM g/L	IgE IU/Ml	C_3 mg/L	C_4 mg/L
Newborn	7.5- 15.0	0- 010	0- 0.20	0.04- 1.28	57- 116	6.6- 23
1- 3 Months	2.7- 7.5	0.06- 0.58	0.12- 0.87	0.08- 6.12	62- 131	8.7- 27
4- 6 Months	1.9- 8.6	0.10- 0.96	0.25- 1.00	0.44- 16.3	74- 170	8.7- 42
7- 12 Months	3.5- 11.8	0.15- 0.98	0.35- 1.04	0.75- 7.31	74- 170	12- 42
1 - 2 Years	4.0- 12.5	0.35- 1.65	0.40- 1.60	0.75- 16.7	74- 170	9- 34
2- 3 Years	5.0- 13.6	0.45- 1.35	0.45- 1.90	0.75- 29.5	74- 174	9- 34
3- 5 Years	5.4- 14.4	0.50- 2.10	0.50- 2.00	1- 69	80- 180	9- 34
5- 7 Years	5.7- 14.4	0.50- 2.40	0.40- 2.10	1- 161	88- 175	10- 36
7- 12 Years	7.3- 15.1	0.70- 3.25	0.55- 2.10	1.5- 195	89- 195	10- 40

From Comans- Bitter WM et al[11]. Reference values for lymphocytes subpopulations. J Pediatr 2003; 130(3):338-393.

Results:

The results were summarized in 2 figures, and 8 tables. Table (2): showed important physical findings of the study patients. Heart failure, and tachypnea were the main reasons for referral to Pediatric Cardiology department that were present in 90%. Cyanosis was present in 46%, crepitation in 70%, rhonchi in 60%, and clubbing in 24%. Infective endocarditis was present in 12%, pleural effusion in 28%, pericardial effusion in 16%, staphylococcal skin infection in s 4.3%, and history of neonatal septicemia in 2%. Amongst Subgroup IB, there were two dysmorphic cases with Down syndrome as proved by karyotyping.

Table (2) Important physical findings of the study patients (N=50).

Physical Findings	Group I (N=50)		Subgroup IA (N=28)		Subgroup IB (N=22)	
	No. Of Patients	Percentage (%)	No. Of Patients	Percentage (%)	No. Of Patients	Percentage (%)
Tachypnea	45	90%	23	46%	22	44%
Heart Failure	45	90%	23	46%	22	44%
Crepitation	35	70%	17	34%	18	36%
Cyanosis	28	56%	28	56%	-	-
Clubbing	12	24%	12	24%	-	-
Rhonchi	30	60%	10	20%	20	40%
Infective Endocarditis	6	12%	1	2%	5	10%
Pleural Effusion	14	28%	5	10%	9	18%
Pericardial Effusion	8	16%	2	4%	6	12%
Staph.Skin Infection	4	8%	2	4%	2	4%
Neonatal Septicemia	6	2%	1	2%	5	10%
Down Syndrome	2	4%	-	-	2	4%

Table (3): presented the roentgenographic findings in Group I, the radiographic findings, visceral situs solitus was present in 45 patients (90%), while visceral situs inversus was present in 5 patients (10%). The left ventricular configuration and increased cardiothoracic ratio were the main radiological findings of the patients and it was present in 90%. The pulmonary vasculature was increased in 44% of patients and decreased in 10%. There was evidence of radiologic chest infection in the form of bronchopneumonic patch in 70% of patients, pericardial effusion in 16%, and pleural effusion in 28%.

Table (3) Roentgenographic findings in Group I (N=50).

Variables	No.	Percentage%
Visceral Situs Solitus	45	90%
Visceral Situs Inversus	5	10%
Increased C/T Ratio	45	90%
Left Ventricular Configuration	45	90%
Plethoric Lung	22	44%
Oligemic Lung	5	10%
Bronchopneumonic Patch	35	70%
Pleural Effusion	14	28%
Pericardial Effusion	8	16%

Table (4), (5) demonstrated two dimensional echocardiographic diagnoses of various CHD included in the study (number, and percentage) out of the total.

Table (4)

Echocardiographic Findings of Subgroup IA (n=28)	Number	Percentage (%)
TGA Without PS	3	6%
TF	4	8%
Ta+Vps+Tga	1	2%
Ivs + Pa	2	4%
Valvular PS + PFO	2	4%
Peripheral pulmonary branch stenosis+ small PDA	1	2%
TGA + VSD with/without PDA	4	8%
Complex cardiac disease dextrocardia associated with other congenital cyanotic cardiac anomalies)	6	12%
VSD + ASD + pulmonary vascular disease	3	6%
Tapvc + Asd + Pda	2	4%

Table (5)

Echocardiographic Findings of Subgroup IB (n=22)	Number	Percentage (%)
VSD	9	18%
PDA	6	12%
Complete AV Canal + PDA	2	4%
PDA + coarctation of aorta + subaortic stenosis	1	2%
Asd + Papvc	2	4%
Partial AV canal + left AV valve insufficiency	2	4%

Table (4), (5) demonstrated two dimensional echocardiographic diagnoses of various CHD included in the study (number, and percentage) out of the total. Ventricular septal defect (VSD) was the commonest lesion (18%) followed by Tetralogy of Fallot (ToF; 8%), atrial septal defect (ASD;8%), patent ductus arteriosus (PDA; 12%), transposition of great arteries (TGA; 14%), partial or total A-V canal 8%, aortic stenosis (AS; 4%), and valvular pulmonic stenosis (PS), ricuspid atresia (TA), partial, and total anomalies pulmonary venous drainage, single ventricle with pulmonic stenosis (SV with PS) and Peripheral pulmonary branch stenosis+ small PDA in 1%. Complex cardiac disease (dextrocardia

associated with other congenital cardiac anomalies) was present in 12%.

Table (6) blood analysis for subgroup IA versus subgroup IB

Variables	Subgroup IA		Subgroup IB		Total		P- Value
	No.	%	No.	%	No.	%	
Leucocytosis (High TLC)	20	40%	17	34%	37	74%	0.26
Anemia (Low HB)	21	52%	19	38%	45	90%	0.43
Polycythemia(High HT).	5	10%	-	-	5	10%	0.12
Iron Deficiency Anemia	26	52%	19	38%	45	90%	0.001*
Low Serum Calcium	15	30%	18	36%	33	66%	0.1

Table (6) showed that, blood analysis for subgroup IA versus subgroup IB. Complete blood pictures was done for studied patients and it was revealed that, the total leucocytic count was high in 74% of total cases. the hemoglobin percentage ranged between 8.5 gm% and 12.5 gm% with a mean of 10.5± 2.1 gm%, while the hematocrite values varied between 17 gm% and 25 gm% with a mean of 21 ± 4.1 gm%. In subgroup IA, polycythemia was present in 10%, while iron deficiency anemia was present in 90% of Group I.

Table (7): Comparison of the immunological profile of subgroup IA, IB and Group II.

Variables	Subgroup IA (N= 28)	Subgroup IB (N= 22)	Control Group (N= 50)	F	P
	Mean ±SD	Mean ±SD	Mean ±SD		
C_3 (IU/ml)	90 ±75.26	111 ±23	119 ±10.05	1.8	0.19
C_4 (IU/ml)	32 ±29.76	25.3 ±4.88	20.68 ±1.93	3.7	0.028*
IgA (mg/dl)	86 ±86.97	72.7 ±14.39	19 ±4.2	7.78	0.001*
IgM (mg/dl)	205 ±112	183 ± 114	79.88 ±21.1	26.14	0.001*
IgG (mg/dl)	1555 ±814	1443 ±185.8	578 ±21.7	30	0.001*
IgE(IU/ml)	91 ±46	64 ±25.7	3.57 ±0.49	8.38	0.001*

By using analysis of variance "ANOVA" Table (7) shows that compared cyanotic Group with non cyanotic Group, and control Group as regards serum levels of IgG, IgA, IgM, IgE, and C_4. There was a higher statistically significant difference between the three studied groups.

Table (8): Frequency of normal, high, low levels of serum immunoglobulin and serum complement levels in Group I.

Levels	Serum Igg (Mg/Dl)		Serum Igm (Mg/Dl)		Serum Ige (IU/ Ml)		Serum Iga (Mg/Dl)		Serum C_3 (IU/ml)		Serum C_4 (IU/Ml)	
	No.	%	No.	%	No.	%	No.	%	No	%	No.	%
High	31	62%	23	46%	10	20%	-	-	7	14%	11	22%
Normal	18	36%	26	52%	40	80%	49	98%	21	42%	29	58%
Low	1	2%	1	2%	-	-	1	2%	22	44%	10	20%

Table (8): presented frequency of normal, high, low levels of serum immunoglobulin and serum complement levels in Group I. Serum IgG level was high in 31 cases (62%), normal in 36%, and low in 2% out of the studied cases. Serum IgM level was high in 46%, normal in 52%, and low in 2% Serum IgE level was high in 20%, and normal in 80%. Serum IgA level was high in 98%, and low in 2% out of the studied cases out of the studied cases. Serum C_3 level was high in 14%, normal in 42%, and low in 44%, and Serum C_4 level was high in 22%, normal in 58%, and low in 20% out of the studied cases.

In the non-parametrical correlation analysis, figure (1) showed a correlation between age in months, and serum C_4 concentration in immunologically evaluated patients ($r=0.56, p<0.05$)

Figure (1): Correlation between age in months, and serum C_4 concentration in immunologically evaluated patients ($r=0.409$, $p<0.001$)

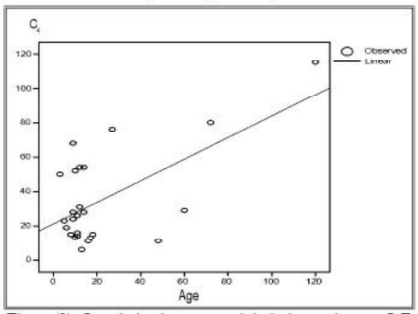
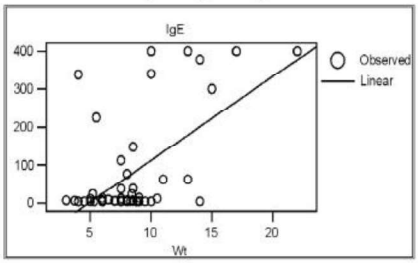


Figure (2): Correlation between weight in kgs and serum IgE concentration in immunologically evaluated patients ($r=0.57$, $p<0.05$).



Discussion:

Congenital heart diseases (CHD) are common pediatric problems that exist primarily at birth. They are characterized by gross structural abnormalities of the heart or the great vessels that actually interfere with normal cardiac function[1].

Immunodeficiency in association with CHD was first recognized in Di-George syndrome[2]. Recurrent infections are not limited to the chest, but usually involving the gastrointestinal tract, urinary tract and the skin. Immunodeficiency is clinically suspected in case of unusually recurrent or unusually severe infections. Normal pre-school children may experience as many as six to twelve minor infections a year. Those who have severe, persistent, atypical or additional infections should be investigated for an underlying cause. Predisposing factors such as poor hygiene and malnutrition can exacerbate the problem[12].

The clinical diagnosis of a probable immunodeficiency disease is based on a variety of criteria, such as history of recurrent infections, the pattern of infections, length of time to clear infections, types of infecting organisms, particularly when involving opportunistic or unusual organisms, and responses to antibiotic therapy[13]. Evaluation of immune function should be initiated for children with clinical manifestations of a specific immune disorder or with unusual, chronic, or recurrent infections[14].

The present study was performed on 50 sick infants and children with established congenital heart diseases (Group I). They were previously hospitalized with unusual chronic recurrent infections, either in the form of chronic otitis media, infective endocarditic, abscesses, brain abscesses, sepsis, recurrent chest infections as pneumonia, pleural, pericardial effusion, and empyema.

The studied patients were subclassified into under two main subgroups: subgroup IA (cyanotic) 56%, and subgroup IB (acyanotic) 44%.Ventricular septal defect (VSD) was the commonest lesion (18%) followed by transposition of great arteries (TGA; 14%), patent ductus arteriosus (PDA; 12%), Tetralogy of Fallot (ToF; 8%), atrial septal defect (ASD;8%), partial or total AVcanal 8%, aortic stenosis (AS; 4%), and valvular pulmonic stenosis (PS),tricuspid atresia (TA), partial, and total anomalies pulmonary venous drainage, single ventricle with pulmonic stenosis (SV with PS) and Peripheral pulmonary branch stenosis+ small PDA (1%). Complex cardiac disease (dextrocardia associated with other congenital anomalies) were present in 12%.Amongst subgroup IB, there were two dysmorphic cases, who had Down syndrome as proved by karyotyping.

The radiographic findings our patients showed that, visceral situs solitus was present in 45 (90%) of patients, while visceral situs inversus was present in 10% of patients. The left ventricular configuration and increased cardiothoracic ratio were the main radiological findings of the patients and it was present in 90% of patients. The pulmonary vasculature was increased in 70% of patients and decreased in 10% of patients. There was evidence of radiologic chest infection in the form of bronchopneumonic patch in 70% of patients, pericardial effusion in 10% of patients, and pleural effusion in 18% of patients. Heart failure, and tachypnea were the main reasons for referral to Pediatric Cardiology department that were present in 90%. Cyanosis was present in 46%, crepitation in 70%, rhonchi in 60%, and clubbing in 24%. Infective endocarditis was present in 12%, pleural effusion in 28%, pericardial effusion in 16%, staphylococcal skin infection in s 4.3%, and history of neonatal septicemia in 2%. Our findings concerning serum immunoglobulins are in accordance with[15].

Amongst Subgroup IB, there were two dysmorphic cases with Down syndrome as proved by karyotyping.

Complete blood pictures was done for these patients and it was revealed that, the hemoglobin percentage ranged between 8.5 gm% and 12.5 gm% with a mean of 10.5± 2.1gm%, while the hematocrite values varied between 17% and 25% with a mean of 21 ± 4.1%. Effort should be made to maintain hemoglobin levels at above normal levels by iron supplements and transfusion if necessary particularly at the time of cardiac catheterization, because relative anemia is much more dangerous than polycythemia. Iron deficiency anemia was present in 45 (90%) of 50 cases with congenital heart diseases.

The mean levels of IgG, IgM, IgE immunoglobins were significantly higher in the subgroup IA compared to either the subgroup IB or the control Group. Girls had significantly higher IgM and IgG levels than boys. Serum IgG level was high in 31 cases (62%), normal in 36%, and low in 2% out of the studied cases. Serum IgM level was high in 46%, normal in 52%, and low in 2% Serum IgE level was high in 20%, and normal in 80%. These children had normal stool culture and normal eosinophilic count. Serum IgA level was high in 98%, and only one acyanotic case had low serum IgA level, and he was diagnosed by karyotyping as Down syndrome. Serum C_3 level was high in 14%, normal in 42%, and low in 44%, and Serum C_4 level was normal in 58%, low in 20%, high in 22%, and these findings were being suggestive of the presence of chronic infections. The low serum complement levels may contribute to their increased susceptibility to infections. Our findings concerning serum immunoglobulins are in accordance with[16], who found that, usually all three major classes of immunoglobulins (IgG, IgM, IgA) are elevated in severely malnourished, althought increases in a single class IgA or IgE have been noted. During specific infections, immunoglobulins levels become further elevated.

As regards high serum immunoglobin values, the high serum levels of IgG may mean a long-term (chronic) infection, is present. While high serum levels of IgM can mean macroglobulinemia, early viral hepatitis, mononucleosis, kidney damage (nephrotic syndrome), or a parasite infection is present. Because IgM antibodies are the type that form when an infection occurs for the first time, high levels of IgM can mean a new infection is present. High levels of IgM in a newborn mean that the baby has an infection that started in the uterus before delivery.A high level of IgE can mean a parasite infection is present. Also, high levels of IgE are

found in people who have allergic reactions, asthma, atopic dermatitis[4].

Some people are born with low or absent levels of IgA antibodies. Low levels of IgA occur in kidney damage (nephrotic syndrome), a problem with the intestines e.g. enteropathy. While low levels of IgG occur in macroglobulinemia. In this disease, the high levels of IgM antibodies stop the growth of cells that make IgG. Other conditions that can cause low levels of IgG include a type of kidney damage (nephrotic syndrome). In rare cases, some people are born with a lack of IgG antibodies. These people are more likely to develop infections. Low levels of IgM occur in some inherited types of immune diseases. Low levels of IgE can occur in a rare inherited disease that affects muscle coordination (ataxia-telangiectasia)[17].

Our findings concerning serum IgG, IgA levels were not in accordance with Khalil, et al.,[18], who stated that immunoglobulins IgG and IgA levels are significantly reduced in all children with congenital heart disease and history of repeated chest infection, whereas IgM levels were increased in cyanotic but unaffected in the acyanotic Group. Complement C_3 and C_4 levels were reduced in all, more so in cyanotics.

Patients with a defect in C_3 (the deficiency in the lytic component of the complement cascade) are at high risk for recurrent infection with Neisseria gonorrhoeae or Neisseria meningitides, severe pyogenic infections, and sepsis[19].

Conclusion:

The immunological evaluation of patients suffering from CHD and recurrent usual infections is warranted. Since it is heralded by immune dysfunction, usually manifest as high serum levels of immunoglobin, and low serum complement levels. Early and accurate diagnosis of such immune dysfunction is essential to ensure that optimal treatment is given and to minimize the risk of progressive or irreversible lung damage. There is a clear evidence of an association between malnutrition, poor wound healing, impaired immunity, and an increased risk of pneumonia.

References:

1. Allen, Hugh D.; Driscoll, David J.; Shaddy, Robert E.; Feltes, Timothy F. Moss and Adams' Heart Disease in Infants, Children, and Adolescents: Including the Fetus and Young Adults, 7th Edition, 2008
2. Di-George AM: Congenital absence of the thymus and its immunological consequence: Concurrence with congenital hypo-parathyroidism. Birth defects, 1968; 4:116 -121.
3. Mancini G, Carbonard AD, Mermans JF: Immunological profile in CHD Immunochemical quantitation of antigen by single radial immunodiffusion. Immuno-chemistry 2005, 2: 235.
4. Berger M, Frank MM: The serum complement system. Immunologic Disorders in Infants and Children, 5th ed. Philadelphia: WB Saunders; 2005: 157- 187.
5. Welte K, Dale D: Pathophysiology and treatment of severe neutropenia. Ann Hematol 2005; 72: 158-165.
6. Ballow, M. Approach to the patient with recurrent infections. Clin Rev Allergy Immunol 2008; 34:129.
7. Dukes RJ, Rosenow EC, Hermans PE: Pulmonary manifestations of hypogamma-globulinemia Thorax 33:603 -607, 1998
8. Goodkin HP, Harper MB, Pomeroy SL: Intracranial abscess in children: Historical trends at Children's Hospital Boston. Pediatrics 2004; 113:1765-1770
9. Moreillon P, Que YA: Infective Endocarditis. Lancet 2004; 363:139-148.

10. Valente AM, Jain R, Scheurer M, et al: Frequency of infective endocarditis among infants and children with Staphylococcus aureus bacteremia. Pediatrics 2005; 115: 15-19.
11. Comans Bitter WM et al: Immunophenotyping of blood lymphocytes in childhood. Reference values for lymphocytes subpopulations. J Pediatr 2003; 130 (3):338-393.
12. Sorensen RU, Butler B, Leiva LE: A review of the immune system: Methodology for evaluating the impact of nutrition on its function. In Suskind R, Tontisirin K (eds): Nutrition, immunity and infection Philadelphia, Lippincott, Williams & Wilkins, in press, 2000.
13. Lindegren M. L, Kobrynski L, Rasmussen SA: Applying public health strategies to primary immunodeficiency diseases: A potential approach to genetic disorders. Recomm Rep 2004; 53:1-29.
14. Regelman WE: Diagnosing the cause of recurrent and persistent pneumonia in children. Pediatr Ann. 2008; 22:561-568.
15. Braunwald E, Perloff JK, Zipes DP, Libby P, et al: Physical examination of the heart and circulation. Heart disease, 6th ed. Philadelphia, WB Saunders, 2001, pp4-81.
16. Rosenthal A, Olson AD. Malnutrition in hospitalized children with congenital heart disease. Arch Pediatr Adolesc Med 1995; 149: 1098-1102.
17. Kerr, A. R., Paterson, G. K., Riboldi-Tunnicliffe, A., Mitchell, T. J. Innate Immune Defense against Pneumococcal Pneumonia Requires Pulmonary Complement Component C_3. Infect. Immun. 2005; 73: 4245-4252
18. Khalil A, Trehan R, Tiwari A, Malik R, Arora R: Immunological profile in congenital heart diseases. Indian Pediatr, Mar 1994; 31(3):295-300.
19. Vogel, U., Claus, H., von Muller, L., Bunjes, D., Elias, J., Frosch, M. Bacteremia in an Immunocompromised Patient. Clin. Microbiol. 2004; 42: 2898-2901

الملخص

تقييم الحالة المناعية فى الاطفال المرضى بعيوب خلقية بالقلب

تعتبر العيوب الخلقية بالقلب من اكثر الامراض شيوعا وتعرف على انها تحدث فى صورة "خلل هيكلى للقلب أو الشرايين الدموية الكبيرة التى هى فى الواقع ذات أهمية وظيفية". فالأطفال الذين يعانون من العيوب الخلقية بالقلب هم أكثر عرضة للإصابة بالجهاز التنفسى بصفة خاصة، وقد كان أول من إعترف بوجود هذا الارتباط بين العيوب الخلقية بالقلب ووجود خلل فى خلايا جهاز المناعة فى المرضى الذين يعانون من متلازمة ديجورج حيث وجد انخفاض فى الاجسام المناعية س٣، س٤، وخلايا التاء.

عينة الدراسة:

فى دراستنا تم اختيار الحالات على اساس وجود بعض الاضطرابات الغير عادية مثل الالتهابات المزمنة المتكررة؛ مثل الالتهابات البكتيرية المتكررة الخطيرة (ثلاثة أو أكثر فى السنة) وايضا حدوث أمراض الجهاز التنفسى الخطيرة الناتجة عن مونلة البكتيرية الناعمة والتهابات الأنسجة الخلوية، والتهاب الأذن الوسطى، أو التهاب الغدد الليمفاوية فى غضون سنة واحدة ؛ وتم اختيار خمسين من ثلاثمائمة حالة من الأطفال (الفئة العمرية ٤- ٣٣ شهرا) مصابين بأمراض عيوب القلب الخلقية وتم تشخيصهم بناء عن التاريخ المرضى للحالة، والفحص البدنى، وقد تم عمل اشعة الصدر ورسم القلب الكهربائى، ودوبلر على القلب.

وتمت دراسة المرضى الذين يعانون من أمراض القلب الخلقية تحت مجموعتين رئيسيتين هما:

- المجموعة الاولى وهم من المرضى الذين يعانون من أمراض عيوب القلب الخلقية المصحوبة بوجود زرقة و(عددهم= ٢٨)
- المجموعة الثانية ٢ (عددهم= ٢٢) وهم من المرضى الذين يعانون من أمراض عيوب القلب الخلقية الغير مصحوبة بوجود زرقة.

فوجد أن ٤٢ من ٥٠ طفلا تقل أعمارهم عن سنتين من ٢٣ ذكور و١٩ إناث (بنسبة ١: ١,٢) ثمانية من ٥٠ طفلا كانوا فوق سن ٢ سنة (٣ ذكور و٥ اناث)

أهم النتائج:

أظهرت النتائج وجود ارتفاع فى الاجسام المناعية ا، ج، م، ى، ووجود انخفاض فى س٣ وس٤، ونقص الهموجلوبين ونسبة الحديد والكالسيوم وارتفاع نسبة الكرات الدموية البيضاء فى جميع الأطفال الذين يعانون من أمراض القلب ووجد ان هذة التغيرات كانت اكثر وضوحا عند مقارنة المجموعتين السابقتين بالمجموعة الضابطة المكونة من نتائج معملية مستخدمة عالميا من اطفال اصحاء من نفس الفئة العمرية والجنس والثقافة. كما ان الدراسة تشير الى ارتفاع نسبة الاطفال الذين تعرضوا لحدوث فشل فى وظائف القلب .

ويلخص البحث مدى اهمية تقييم الحالة المناعية اكلينيكيا ومعمليا فى الاطفال المرضى بعيوب القلب الخلقية والتهابات رئوية متكررة والانيميا الناتجة عن نقص الهموجلوبين ونسبة الحديد والكالسيوم بالدم ومدى اهمية التشخيص والعلاج المبكر لمثل هذة الحا لات لتفادى حدوث تدهور وفشل فى وظائف القلب والرئتين والذى يؤدى بالتالى حدوث تدهور شديد فى الحالة الصحية للطفل.