



Are routine detailed screening tests in healthy children necessary?

Sağlıklı çocuklarda ayrıntılı tarama testleri gerekli mi?

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ABSTRACT

Background: The aim of the study was to determine if routine detailed screening tests in healthy children are needed or not. **Methods:** A total of 590 healthy children (mean age: 9.7±2.9 years, M/F: 286/304) who were referred from primary care providers for screening tests were evaluated retrospectively in terms of laboratory findings such as complete blood count, lipid profiles, liver and kidney function tests. **Results:** Iron deficiency anemia was significantly more common in teenage girls than boys. Only 16.7% of girls and 16.4% of boys had lipid abnormalities. The other biochemical parameters were within normal limits in both groups. **Conclusions:** No significant difference was observed in biochemical parameters in healthy children. Thus, unnecessary tests should not be done in healthy children by primary care physicians. **Key words:** Healthy children, screening tests, biochemical tests

ÖZET

Amaç: Çalışmanın amacı sağlıklı çocuklarda rutin ayrıntılı tarama testlerine gerek olup olmadığını değerlendirmektir. **Gereç ve yöntem:** Çalışmaya aile hekimleri tarafından tarama testlerinin yapılması için tarafımıza yönlendirilen 590 sağlıklı çocuk (ortalama yaş: 9.7±2,9 yıl, E/K:286/304) alınmıştır. Çalışılan test sonuçları (tam kan sayımı, lipit düzeyleri, karaciğer ve böbrek fonksiyon testleri, tiroid testleri) retrospektif olarak değerlendirilmiştir. **Bulgular:** Demir eksikliğine bağlı anemi ergen kız çocuklarında erkeklere oranla daha sık saptanmıştır. Lipit bozuklukları kızlarda %16,7, erkeklerde %16,4 oranında saptanmıştır. Diğer biyokimyasal parametreler normal tespit edilmiştir. **Sonuç:** Sağlıklı çocuklarda ayrıntılı biyokimyasal testler açısından istatistiksel olarak anlamlı patoloji saptanmamıştır. Bu nedenle, maliyet de düşünüldüğünde aile hekimleri tarafından gereksiz testler istenilmemeli ve bu konuda aile hekimleri bilgilendirilmelidir. **Anahtar kelimeler:** Sağlıklı çocuk, tarama testleri, laboratuvar testleri

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INTRODUCTION

Screening is defined as testing for the disease in an apparently healthy population or individual.¹ The goal of screening is not to detect disease in individuals but to identify persons who are at greater risk of having the disease and who warrant further testing.¹ All newborns should be screened for the presence of certain diseases such as congenital hypothyroidism, phenylketonuria (PKU), hyperbilirubinemia and hearing loss.

Pediatric preventive care guidelines recommend periodic health evaluation to assess children's overall health and risk factors for preventable diseases by history, physical exam, age-appropriate developmental assessment, assessment of immunization status and administration of immunizations and laboratory testing as needed.²⁻¹¹ Periodic health evaluation should be done annually between ages 5-21.

Children without symptoms of disease, generally do not need detailed laboratory screening tests. In this study, healthy children who were referred to our hospital from their primary care physicians for laboratory tests were evaluated and the necessity of these tests was discussed.

MATERIALS AND METHODS

A total of 590 healthy children admitted to the pediatric outpatient clinics of Istinye State Hospital (Istanbul, Turkey) between February 2018 and March 2018 were evaluated retrospectively. The children were excluded if they had chronic illnesses such as liver diseases, endocrine, gastrointestinal, cardiovascular or neurological disorders.

Baseline complete blood count, biochemical tests including alanine aminotransferase (ALT), aspartate aminotransferase (AST), fasting glucose, blood urea nitrogen (BUN), creatinine, iron, ferritin, lipid profile, thyroid-stimulating hormone (TSH), free T4 and anti-HBs levels were the screening tests requested by the primary care physicians. Complete blood count was examined by using Mindray BC-6800 (Mindray, China) and biochemical tests were

analyzed by using Beckman Coulter AU680 (Beckman Coulter, Brea, CA, USA).

Children who had hemoglobin levels lower than 11.5 g/dL between 5-11 years of age and 12 g/dL between 12-15 years of age, serum ferritin level lower than 12 ng/ml, iron level lower than 30 µg/dL, iron binding capacity greater than 480µg/dL was regarded as having iron deficiency anemia.^{12,13}

Fasting glucose of 100 to 125 mg/dL (5.5 to 6.9 mmol/L) is considered to be prediabetic (impaired fasting glucose) and a level of ≥ 126 mg per dL (7.0 mmol/L) is consistent with the diagnosis of diabetes.¹⁴

Abnormal values compatible with dyslipidemia are a fasting total cholesterol of ≥ 200 mg/dL, a LDL cholesterol of ≥ 130 mg/dL, non-HDL cholesterol of ≥ 145 mg/dL, triglycerides of ≥ 100 mg/dL for ages 0-9 and ≥ 130 mg/dL for ages 10-19 years and a HDL cholesterol of < 40 mg/dL.¹⁴

Individuals with anti-HBs levels of 10 mIU/mL or greater after completing an HBV vaccination series are considered protected from hepatitis B.^{15,16}

The study has been carried out in accordance with the principles of the Declaration of Helsinki.

Statistical analysis

Statistical analysis was performed using the NCSS (Number Cruncher Statistical System) 2007&PASS 2008 Statistical Software (Utah, U.S.A). All results are expressed as the mean \pm SD. The analysis was conducted using Fisher's exact test and chi-square test. A value of $p < 0.05$ was considered statistically significant

RESULTS:

The mean age of the children was 9.7 ± 2.9 years (range 5-16 years) and male:female ratio was 286/304. 27 (8.8%) of the girls and 10 (0.4%) of the boys had iron deficiency anemia ($p=0.03$) and oral iron therapy was initiated for these children.

Table 1. The demographic features and laboratory findings of the children according to gender			
	Male (n=286)	Female (n=304)	p
Age (mean±SD)	9.63±2.9	9.98±3.0	0.10
Fasting glucose (mg/dL)	94.5±6.5 (95)	93.5±6.5 (94)	0.00
ALT (U/L)	19.3±7.8 (17)	18.1±8.5 (15)	0.00
AST (U/L)	26.9±6.0 (26)	26.5±5.7 (24)	0.41
BUN (mg/dL)	23.5±5.1 (23)	22.8±6.7 (22)	0.10
Creatinin (mg/dL)	0.43±0.0 (0.42)	0.43±0.0 (0.4)	1.00
Cholesterol (mg/dL)	170.5±29.3 (171)	177.6±121 (168)	0.31
Triglyceride (mg/dL)	76.04±34.4 (70)	79.4±33.4 (74)	0.20
LDL (mg/dL)	103.2±24.3 (100)	102.4±24 (101)	0.61
HDL (mg/dL)	52.6±11.7 (51)	51.6±9.8 (50)	0.21
Hemoglobin (g/dL)	13.02±1.0 (13)	12.6±1.1 (13)	0.00
Ferritin (ng/mL)	22.5±10.3 (20)	20.1±9.7 (19)	0.00
Serum iron (µg/dL)	104±76.5 (75)	123±78.2 (78)	0.00
Iron binding capacity (µg/dL)	305±56.6 (300)	320±74.4 (318)	0.00
TSH (µIM/mL)	2.72±1.15 (2.59)	2.69±1.3 (2.49)	0.70
Free T4 (ng/dL)	0.90±0.24 (0.86)	0.90±0.2 (0.87)	1.00
Anti-HBs (Mik-MEIA)			
<10 (number, median)	3.79±2.3 (54, 2)	3.79±2.3 (54, 2)	0.20
>10 (number, median)	119.5±191.9 (104,52)	119.5±191.9 (104,52)	

Anti-HBs=hepatitis B surface antibody; ALT= alanine aminotransferase; AST= aspartate aminotransferase; BUN= blood urea nitrogen; HDL=high-density lipoprotein; LDL= low-density lipoprotein; TSH= thyroid-stimulating hormone
*Fisher's exact test and chi-square test. p < 0.05 was considered statistically significant.

Only 16.7% of girls and 16.4% boys had lipid abnormalities. 27 (8.8%) of the girls had hypercholesterolemia, 51 (16.7%) had hypertriglyceridemia and 27 (8.8%) had high LDL levels, whereas 32 (11.1%) of the boys had hypercholesterolemia, 47 (16.4%) had hypertriglyceridemia and 26 (9%) had high LDL levels ($p>0.05$) (Table 1). Physical activity and referral to dietitians for appropriate diet were advised to these patients. The other biochemical parameters were within normal limits in both groups (Table 1).

Because the list of screening tests was changed according to a primary care provider, anti-HBs levels were examined in 158 (5.2%) of the boys and 160 (52.6%) of the girls. 65.8% of the boys and 59.3% of the girls had protective anti-HBs titers.

DISCUSSION

American Academy of Pediatrics (AAP), the CDC (Centers for Disease Control and Prevention), and the U.S. Preventive Services Task Force have recommendations for both universal screening and targeted population-specific screening.²⁻⁷ Height, weight, body mass index, the onset of sexual maturity, iron deficiency anemia, vision and hearing screening, cognitive, emotional and social maturation, immunization are considered mandatory.²⁻¹⁰ The other issues such as latent tuberculosis, lead screening, and dyslipidemia risk assessment should be done on an as-needed basis.

Height and weight should be evaluated at every visit to a primary care physician. Screening for obesity in children 6 years and older and offering or referring them for detailed evaluation if children have BMI \geq 85th percentile or a significant increase in BMI percentile are recommended.^{3,17,18} No evidence was found on appropriate screening intervals for obesity.^{3,17}

The North American Society of Pediatric Gastroenterology, Hepatology, and Nutrition (NASPGHAN) published a clinical practice guideline outlining the screening, diagnosis, and treatment of pediatric nonalcoholic fatty liver disease (NAFLD).¹⁹ They recommend that children older than 10 years with a body mass index (BMI) \geq 85th percentile should be screened for NAFLD

using an alanine aminotransferase (ALT) level.^{19,20} The limitation of our study was that children were evaluated retrospectively, thus BMI could not be calculated. We observed that from not only overweight or obese children but AST and ALT have also been requested from all of the children regardless of BMI.

The U.S. Preventive Services Task Force (USPSTF) concludes that the evidence is insufficient to recommend for or against routine screening for lipid disorders in infants, children, adolescents, or young adults up to age 20 (Grade: I Statement).³ Dyslipidemias are abnormalities of lipoprotein metabolism and include elevations in TC, LDL-C, or triglycerides or deficiencies of HDL-C. These disorders can be acquired or familial; monogenic dyslipidemias are related to genetic conditions such as familial hypercholesterolemia and multifactorial dyslipidemias are due to risk factors including environmental factors such as obesity, diet, or diabetes.³

An expert panel from the US National Heart, Lung and Blood Institute (NHLBI) endorsed by the American Academy of Pediatrics recommended initial lipid screening with fasting lipid profile for children between two and eight years of age with a BMI \geq 95th percentile (or other risk factors for cardiovascular disease, such as family history of dyslipidemia/early cardiovascular disease and/or morbidity in first- or second-degree relatives, history of diabetes, hypertension, or smoking in childhood).^{10,14,21} In 2014, AAP updated the Schedule of screening and assessment for well-child visits as cholesterol screening ages between 5-8 screen if at risk, starting at age 9 screen child at least once if not previously screened, children older than 11 years screen if not screened previously, or if risk factors (family history of premature cardiovascular disease, parent with known lipid disorder, overweight/obese) have changed.^{6,8} Many children with multifactorial types of dyslipidemia will have normal lipid levels in adulthood. Potential harms of screening may include labeling of children whose dyslipidemia would not persist into adulthood or cause health problems.² The American Academy of Family Physicians (AAFP) and USPSTF conclude that the current evidence is insufficient to assess the balance of benefits and harms of screening for lipid disorders in children and adolescents 20 years or younger.^{2,22} We

observed in this study that screening for lipid disorders have been requested from all of the children regardless of determined risk factors by primary care physicians.

Serum hemoglobin is the primary screening test for identifying anemia, it is not sensitive for iron deficiency because mild deficiency states may not affect hemoglobin levels.⁴ Iron deficiency anemia is more common in teenage girls than teenage boys because their bodies are not able to store as much iron, in addition to the loss of blood during menstruation. Insufficient dietary intake and low socioeconomic status are also risk factors for iron deficiency. In our country, the frequency of iron deficiency anemia (IDA) has been reported to range between 15.2% and 62.5% in different studies involving children.¹² The overall prevalence of anemia was found to be 27.6% in Istanbul.²³ Recommended screening for anemia screen those with known risk factors such as excessive menstrual blood loss, low iron intake, or previous diagnosis of iron deficiency anemia annually.

School-aged children should receive age-appropriate immunizations, as well as catch-up immunizations if needed. Children who have completed the hepatitis B vaccination series and have anti-HBs ≥ 10 mIU/mL is considered as having vaccine-induced protection.^{15,16} Anti-HBs levels following vaccination decline over time. Immunocompetent persons remain protected, even if anti-HBs levels decline to < 10 mIU/mL beyond that time, presumably because of persistent cellular immunity and immune memory.^{15,16} In our study, 53% of the children were referred by their primary care physicians for testing anti-HBs levels. The benefit to cost ratio of the tests should be acceptable.

As discussed in these guidelines, no recommendations were mentioned about a routine screening of serum ALT, AST, fasting glucose, BUN, creatinine, iron, ferritin, lipid profile, thyroid function tests, and anti-HBs levels in healthy children.

In conclusion, screening is carried out for early identification and treatment of common childhood diseases and will definitely reduce the incidence of these diseases. Our aim should be to reduce the prevalence of preventable diseases for

healthy generations. The incidence of these conditions, however, varies in countries and even different regions and states of the same country. Increasing awareness secondary to the needs of the state screening should be done according to needs of where the child lives and demographic parameters. The benefits of early diagnosis must be weighed against unnecessary tests and procedures.

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