Laboratory Tests Might Mitigate Misdiagnosis of Child Abuse Established on Clinical Grounds

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Article

Laboratory Tests Might Mitigate Misdiagnosis of Child Abuse Established on Clinical Grounds

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Abstract: Given that evaluating suspected child maltreatment is a challenging task, we aimed to begin to explore how laboratory test results may assist in its detection. Hence, we have examined biomarker differences between 137 children entering out-of-home care and 126 children living in their own homes. Each child entering Majorcan institutionalized care was randomly matched for gender and age with children living in their homes and the same health area. Concerning basic hematological and biochemical values, children placed in out-of-home care differed significantly from children remaining at home in four distinct ways. Children at care entry had significantly higher eosinophil counts than children at home; and also had significantly lower levels of transaminase, thyroid-stimulating hormone, triglycerides and LDL-Cholesterol than children living at home. Oxidative stress linked to anxiety disorders and underweight are common features found in children at entry into the care system. The present study shows a relationship between some underweight or oxidative stress biomarkers and the risk of entry into out-of-home care. Medical diagnoses require physicians to select and assemble relevant data from all available information. Accordingly, we should consider the implementation of laboratory checkups in order to identify the abused from the non-abused child better.

Keywords: child abuse; child growth; child custoody; sentinel health events; oxidative stress; immune responses; aspartate aminotransferase; fatty liver; insulin resistance

1. Introduction

Professor Fanconi was widely criticized in the 20th-century inter-war period for advocating blood tests for children when it was the right thing to do. According to his opponents, this practice was cruel and useless. Even more, they spread the rumor that Fanconi's enthusiasm for laboratory tests was due to his lack of clinical skills. Similarly, blood tests are not currently carried out on children being investigated for suspected abuse because they are considered useless. This routine is challenging to justify given that, as far as we know, research has not found that it is pointless to order laboratory tests to establish a more accurate diagnosis of child abuse, and also bearing in mind that the unresolved ethical tension between the potential consequences of false-negative and false-positive diagnoses forces physicians to shoulder heavy responsibilities [1].

Since child victims of maltreatment may present with nonspecific symptoms, determining whether the first clinical signs have been caused accidentally or represent abuse is often challenging. The majority of studies have examined the environmental, clinical, or radiological signs that play an essential part in the evaluation of suspected child abuse (CAN). Regretfully, none of these are ready yet to serve as a clinically applicable diagnostic criterion for CAN. Therefore, further work remains

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to be done to develop composite diagnostic criteria; combining highly relevant factors seems to be the most promising approach to the risk assessment of these children [2].

Except for older children, most children living within institutionalized care are significantly below standards for growth when compared with their community peers [3]. In this context, a sizeable amount of data demonstrates the hematological consequences of abnormal body weight [5], like the lipid panel or liver enzyme levels [6]. In addition to body weight, stressful early life experiences are associated with dysregulation of the biological profile [7]. In particular, children who experience chronic and extreme stress can exhibit an oxidative imbalance, including an increase in proinflammatory cytokines production and C-reactive protein (CRP) [8]. These findings stimulate research into the use of underweight or oxidative stress biological markers in assessing the risk of CAN.

The present role of laboratory testing is subordinate to the cluster of clinical, parental, social, and cultural factors that play important parts in evaluating suspected CAN. As pointed out by several authors, at the most, the workup of CAN includes the aid of laboratory tests in only four specific situations: toxicology screening, children presenting bruising, fractures, and suspected sexual abuse [4]. The present article aims to begin examining whether simple blood tests linked to body weight or oxidative stress provide an inexpensive and practical method to identify groups at risk of CAN.

2. Materials and Methods

Setting

This study was conducted in the Majorcan residential home intended as temporary institutional placement for children in urgent need of shelter. Should family reintegration prove contrary to the child's best interests, stable solutions are sought.

Study population

All Majorcan children aged 4-14 years deprived of parental care from January 1st, 2012, to December 31st, 2014, were invited to participate in this study. Youths whose legal guardians did not consent to participate or whose medical files did not include laboratory results during the year admission to out-of-home care occurred were excluded.

Household sample

In order to assess the biomarkers of children who entered institutionalized care, each one of these children was randomly matched for gender and age at arrival with children living in their own homes and the same health area. All children whose medical files did not include laboratory results from January 1st, 2012, to December 31st, 2014, were excluded. As usual, the ratio to cases was 1:1. After sampling, study representatives contacted parents and asked permission for the child to participate.

Study design

This project is Part II of a cross-sectional study examining the health status of vulnerable children at entry to out-of-home care [9]. The primary outcome of this part was to report significant variations of serum biochemical or hematological parameters between children at care entry and children at home.

Data collection

The data was collected between May and September 2017 from case files at entry to institutionalized care and duplicate age control files. This data includes scheduled child health program visits and on-demand doctor consultations. All data was entered into a standardized data extraction tool (available upon request).

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Variables

Eleven hematological markers and eighteen biochemical markers were measured. In addition, the following variables were collected in the standardized data extraction tool: perinatal data, sex, date of birth, date of residential placement, and growth parameters. Anthropometric measures of weight, length, and body mass index (BMI) were taken.

Statistical analysis

All analyses were conducted in Microsoft Excel 2007 and SPSS version 16. We compared the results of growth measurements and developmental status between children entering care and those in the general population. Statistical comparisons included paired 2-tailed t-tests, frequency distribution, and regression analysis. The 95% confidence intervals (95% CI) were calculated, and $p < 0.05$ was chosen as the significance level; bivariate analyses were conducted, and unadjusted odds ratios were calculated.

Ethics

Participants were recruited using procedures approved by the Majorcan Committee for Primary Care Research Ethics, and informed consent was obtained before data collection. Ethical approval was obtained from the Regional Institutional Review Board.

3. Results

Table 1. shows that there were no differences between groups for either perinatal or demographic characteristics.

Table 1. Patients' profile by residential type. Mean (standard deviation) unless otherwise stated.

	Looked after children N=137	**Children at home N=126**	**P value**
Weeks of gestation	38.39 (2.70)	38.85 (1.94)	.322
Mean birth weight, g	3090.85 (680.52)	3157.88 (506.96)	.549
Male gender	51.1%	47.6%	.573
Female gender	48.9%	52.4%	
Any breastfeeding	63.30%	61.90%	.870
Years of age at study entry	8.61 (2.96)	9.02 (3.22)	.402

3.1. Growth results (Table 2). No significant differences were found in mean weight or BMI percentiles between children on admission into residential care and children living with their birth family. Nevertheless, children at home were significantly taller than children at care entry. Further examination of anthropometric measurements shows no differences in the number of children at or below the 50th percentile for weight or height, regardless of location of residence. However, data analysis revealed that more than twice the expected number of children on admission into institutionalized care were at or below the 25th percentile for weight or height when compared to children at home (33% versus 17% and 34% versus 14%, respectively). Finally, height below the 10th percentile was three-fold higher among children at care entry than in the population at home (16% versus 5%).

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Table 2. Anthropometric measurements by residential type. Number (%) unless otherwise stated.

Child growth parameters	Children at care entry N=137	Children at home N=126	P value	OR (95%CI) or MD (95%CI)
Weight ≤ percentile 10	5 (10.2)	4 (4.6)	0.293	2.35 (0.60 to 9.23)
Weight ≤ percentile 25	18 (33.3)	15 (17.4)	0.031*	2.36 (1.06 to 5.23)
Weight ≤ percentile 50	34 (63.0)	44 (51.2)	0.171	1.62 (0.81 to 3.25)
Height ≤ percentile 10	7 (16.2)	4 (4.7)	0.042*	3.93 (1.08 to 14.29)
Height ≤ percentile 25	17 (34.0)	12 (14.3)	0.007**	3.09 (1.32 to 7.20)
Height ≤ percentile 50	33 (66.0)	48 (57.1)	0.311	1.45 (0.70 to 3.01)
Weight percentile, mean (S.D.)	53.3 (28.6)	61.5 (26.6)	0.092	-8.2 (-17.76 to 1.36)
Height percentile, mean (S.D.)	50.4 (26.7)	61.6 (24.2)	0.016*	-11.22 (20.33 to -2.12)
BMI percentile, mean (S.D.)	53.2 (28.7)	53.1 (28.0)	0.406	0.12 (-10.16 to 10.40)

ABBREVIATIONS: BMI, body mass index; CI, confidence interval; MD, means difference; OR, odds ratio; S.D., standard deviation; * ≤ 0.05, ** ≤ 0.01.

3.2. Concerning basic hematological and biochemical values, children placed in out-of-home care differed significantly from children remaining at home in four distinct ways. Blood cells: Children at care entry had higher eosinophil counts than children at home. Liver function tests: On admission into care, these children had significantly lower levels of Aspartate aminotransferase (AST) and Gamma-glutamyl transpeptidase (GGT), as well as higher levels of total serum proteins than children at home. Lipid profile: Children at care entry had lower serum concentrations of triglycerides (TG) and low-density lipoprotein cholesterol (LDL-C) than children at home. Hormones: Lower thyroid-stimulating hormone (TSH) levels in children at care entry were also found compared to children at home. No significant differences were found in the concentrations of the rest of the serum biomarkers included in this study (Table 3).

Table 3. Laboratory data. Comparison between children living at home and children at entry into care.

Laboratory variables	Children at care entry N=137	Children at home N=126	P value	OR (95%CI) or MD (95%CI)
Glycaemia, (mmol/L)	4.69±0.45	4.84±0.66	0.361	-0.15 (-0.47 to 0.17)
Total Cholesterol (mmol/L)	3.66±0.70	4.14±0.73	0.079	-0.48 (-1.02 to 0.05)
HDL Cholesterol (mmol/L)	1.18±0.46	1.39±0.52	0.385	0.21 (-0.28 to 0.71)
LDL Cholesterol (mmol/L)	1.18±0.46	2.61±0.54	<0.0001 ***	1.43 (0.92 to 1.94)
Tryglicerides (mmol/L)	0.58±0.14	0.84±0.21	0.001**	-0.26 (-0.40 to -0.11)
Aspartate aminotransferase (microkat/L)	0.34±0.11	0.56±0.14	0.0002**	0.21 (0.11 to 0.32)
Alanine aminotransferase (microkat/L	0.28±0.17	0.36±0.18	0.182	0.80 (-0.03 to 0.20)
Gamma glutamyl transpeptidase (microkat/L)	0.20±0.45	0.56±0.52	0.035*	0.35 (0.02 to
Phophatase, alkaline (microkat/L)	5.85±6.63	4.67±1.56	0.616	-1.18 (-6.12 to 3.76)
Bilirubin (total) (micromol/L)	7.34±.88	9.04±2.95	0.143	1.69 (-0.61 to 4.01)
Protein (total) (grams/L)	95.00±9.29	86.75±7.15	0.045*	-8.25 (-16.30 to

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				-0.20)
Urea (mmol/L)	9.58±2.81	10.40±2.44	0.413	0.81 (-1.19 to 0.81)
Creatinine (micromol/L)	49.35±9.20	49.43±6.21	0.972	0.07 (-4.41 to 4.57)
Serum Sodium (mmol/L)	138.46±1.84	139.52±0.80	0.259	1.06 (-0.81 to 2.93)
Serum Potassium (mmol/L)	4.28±0.54	4.33±0.43	0.763	0.05 (-0.28 to 0.39)
Serum Chloride (mmol/L)	106.50±1.29	107.00±1.41	0.575	0.50 (-1.45 to 2.45)
Red cells count (*10^{12}/L)	4.68±0.32	4.69±0.26	0.858	0.014 (-0.14 to 0.17)
Hemoglobin (g/L)	13.46±1.24	13.48±0.86	0.954	0.01 (-0.56 to 0.59)
Hematocrite (fraction)	39.20±3.41	39.40±2.89	0.817	0.19 (-1.52 to 1.92)
Mean corpuscular volume (fl)	83.72±4.71	83.90±4.76	0.893	0.17 (-2.41 to 2.76)
Leukocyte count (*10^9/L)	8.57±3.07	8.11±3.06	0.541	-0.46 (-1.96 to 1.04)
Neutrophile count (*10^9/L)	4.01±1.71	4.04±1.91	0.943	0.03 (-0.96 to 1.03)
Lymphocyte count (*10^9/L)	3.14 ±1.43	4.64±8.66	0.387	1.50 (-1.95 to 4.95)
Monocyte count (*10^9/L)	0.62±0.34	0.69±0.31	0.405	0.07 (-0.10 to 0.25)
Eosinophil count (*10^9/L)	0.61±0.58	0.31±0.22	0.014*	-0.30 (-0.54 to -0.06)
Platelet count (*10^9/L)	294.31±75.90	322.79±84.90	0.085	38.48 (-5.63 to 82.58)
INR (fraction)	1.06±0.11	1.11±0.06	0.339	-0.04 (-0.01 to 0.04)
Thyroid-stimulating hormone (mIU/L)	1.05±0.20	2.93±0.08	<0.0001 ***	1.88 (1.61 to 2.14)
Thyroxine, free (picomol/L)	13.57±2.57	14.93±1.33	0.388	1.35 (-2.20 to 4.90)

Values are presented as number (%) or means ± standard deviations, unless otherwise stated. ABBREVIATIONS: CI, confidence interval; INR, International Noramlized Ratio; kat, katal or unit of catalytic activity; L, liter; MD, means difference; mIU, milliinternational units; mmol, milimols; OR, odds ratio; * ≤ 0.05, ** ≤ 0.001, *** ≤ 0.0001.

4. Discussion

This regional study examined the association between entry into institutionalized care and a range of laboratory parameters. We found a discrepancy in laboratory characteristics between children at home and children at care entry, where the latter were significantly thinner and shorter than children at home. Our results are from previous research that lower levels of selected biomarkers are associated with lower body weight.

Blood cells. The absolute eosinophil count of children on admission into care doubles that of controls (0.61±0.58 versus 0.31±0.22*109/L) and falls beyond the upper limit for this parameter (0-0.45*109/L) [10]. Our results agree with prior observations that linked higher levels of home stress or perceived threat with higher eosinophil counts [11]. Conversely, other authors have found a progressive increase in neutrophil count (not exceeding the accepted physiological range) as the BMI increased [12]; these findings agree with the connection between peripheral blood leukocytosis and low-grade inflammatory states. However, this is not shown in our results.

Lipid profile. Children at care entry, while within the normal range, had lower serum concentrations of TG (0.58±0.14 versus 0.84±0.21 mmol/L) and LDL-C (1.18±0.46 versus 2.61±0.54 mmol/L) than children at home. Combined evidence from cohort studies indicates that, even in children, there is a direct relationship between increased weight and higher blood lipid levels. In our study, higher TG and LDL-C levels were linked to higher weight scores, which concur with data reported in other populations [13].

Hormones. We report significant variations of serum TSH within the reference range between children at care entry and children at home (1.05±0.20 versus 2.93±0.08 mIU/L). This finding was expected since weight reduction is a unique predictor of decreased TSH [14,15]. C-RP level variation mediates this association. Unfortunately, C-RP was not available in our sample.

Liver function tests. Over two decades, a number of both cross-sectional and longitudinal analyses have found persistent hypertransaminasemia resolving after weight reduction in children.

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The hepatic abnormalities of unknown origin identified in one series of obese children showed a persistent improvement that paralleled the loss of excess weight [16], and a large longitudinal study on overweight children has demonstrated that 16% of children in the weight reduction intervention group had elevated transaminases versus 30% of children without intervention [17]. On the opposite end of the weight spectrum, we have also found that AST or GGT levels of children with proper weight living in their own homes are approximately double that of underweight children entering institutionalized care (0.56±0.14 versus 0.34±0.11 microkat/L, and 0.56±0.52 versus 0.20±0.45 microkat/L, respectively).

The data mentioned above reintroduces the assumption that the oxidative stress induced by an accumulation of fat within the liver predisposes hepatocyte inflammation and subsequent increased AST release from dying hepatocytes [18]. This adds even more weight to the argument that a trial period of lifestyle modification is appropriate in case of mildly elevated transaminase levels [19].

We have also found significant differences in plasma protein levels between children at care entry and home (95.00±9.29 versus 86.75±7.15 gram/L). Plasma protein levels of children at care entry highly exceed the upper limit of the normal range of this parameter [20]. Given that the plasma proteome contains proteins from various cellular localizations with specific roles in a wide range of functions, the implications of our findings remain to be determined.

We are aware of the harmful repercussions that can ensue from CAN overlooking or misdiagnosis. What is less openly acknowledged is that clinical practice sometimes forces us to decide which outcome is more critical to avoid. Therefore, to meet our ethical obligations, we have used as many tools as were available to us despite needing more evidence of the validity of some of them. One such situation occurs with expert opinion. On the one hand, we know that CAN-specialized pediatricians and clinicians who regularly perform CAN examinations and review cases with an expert reach greater knowledge and competence in interpreting findings in CAN [21]. However, it should also be emphasized that when the findings are unmistakably normal or abnormal, experts reach a consensus; conversely, when the diagnosis is less clear-cut, they show wide diagnostic variability results [22]. Finally, despite the multiplicity of scores aimed at detecting CAN, the authors of a recent review analyzed only seven of these questionnaires in detail with a low risk of bias. They found that sensitivity ranged between 0.72 and 0.80 and specificity between 0.84 and 0.98. They conclude that there is no scale for early diagnosis and that the validity of the inquiry may be increased by combining multiple tests [23].

The lack of tests that would aid in the accurate diagnosis of CAN keeps us in the controversy between a significant number of false claims of CAN and the severe repercussions of missing CAN. Given that it is imperative to confront the matter, it will only be justified to stop exploring the role of laboratory results in this diagnosis if proven useless in identifying CAN.

LIMITATIONS

This is an observational study of less than three hundred children. Hence, our results only apply to some populations. Of the studies reviewed, children living within institutionalized care were commonly malnourished, with undernutrition affecting young children particularly. Our sample covers a wide age range (4-14 years). The wide variety of conditions in which anthropometry of institutionalized children was reported does not allow for optimal sample size calculation, and the low number of laboratory results precludes a multivariate analysis of our data.

There are several possible explanations for any patterns found. This study cannot establish whether these associations reflect background risk factors that predate out-of-home care placement. In addition, at the time of writing, there was no vast body of literature to provide indirect or robust support to the values found in this survey.

Finally, since previous reports support a linear relationship between body weight and blood levels of hormones, lipids, or liver enzymes, we must acknowledge that “underweight” is a generally problematic variable.

5. Conclusions

In studying institutionalized children, we found lower levels of cholesterol, transaminase, and TSH among children at care entry than among children at home. This short report raises a new issue about institutionalized children; not only are they significantly thinner and shorter than children living at home, but the use of blood biomarkers can improve our understanding of the complex processes through which these children must go.

As part of the effort that is being made to identify the abused from the non-abused child, we would like to stress that more work is needed to disentangle further the complex interrelations between biological profiles and the risk of child abuse.

Author Contributions: Study conceptualization and design: SV. Acquisition, analysis, or interpretation of data: LlS and A-ET. Literature review and drafting of the first manuscript: SV and ES. A-ET had full access to all the data in the study and took responsibility for the integrity of the data. All authors approved the final manuscript for submission.

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Institutional Review Board Statement: Participants were recruited using procedures approved by the Majorcan Committee for Primary Care Research Ethics, and informed consent was obtained before data collection. Ethical approval was obtained from the Regional Institutional Review Board.

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study

Data Availability Statement: The data underlying the findings can be obtained upon request from the corresponding investigator.

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References

1. Brown, S.D. Ethical challenges in child abuse: what is the harm of a misdiagnosis?. *Pediatr Radiol,* **2021**, *51,* 1070–1075.
2. Jordan, K.; Wild,T.; Fromberger,P.; Müller,I.; Müller,J.L. Are There Any Biomarkers for Pedophilia and Sexual Child Abuse? A Review. *Front Psychiatry.* **2020,***10,*940.
3. DeLacey, E.; Tann, C.; Groce, N.; Kett, M.; Quiring, M.; Bergman, E.; Garcia, C.; Kerac, M. The nutritional status of children living within institutionalized care: a systematic review. *PeerJ.* **2020,** *8*, e8484.
4. Greco,C. From Victim to Minister's Advisor: A Personnal View of Child Protection in France. *Front Pediatr.* **2021,***9,*587806.
5. Purdy,J.C.; Shatzel,J.J, "The hematologic consequences of obesity." *Eur J Haematol.* **2021**,*106*,306-319. doi:10.1111/ejh.13560
6. Bussler, S.; Vogel, M.; Pietzner, D.; Harms, K.; Buzek, T.; Penke, M.; Händel, N.; Körner, A.; Baumann, U.; Kiess, W.; Flemming, G. New pediatric percentiles of liver enzyme serum levels (alanine aminotransferase, aspartate aminotransferase, γ-glutamyltransferase): Effects of age, sex, body mass index, and pubertal stage. *Hepatology*. **2018**,*68*,1319-1330.
7. Lee, C.; Coe, C.L.; Ryff, C.D. Social Disadvantage, Severe Child Abuse, and Biological Profiles in Adulthood. *J Health Soc Behav*. **2017**,*58*,371-386.
8. Danese, A.; Caspi, A.; Williams, B.; Ambler, A.; Sugden, K.; Mika, J.; Werts, H.; Freeman, J.; Pariante, C. M.; Moffitt, T. E.; Arseneault, L. Biological embedding of stress through inflammation processes in childhood. *Mol Psychiatry*. **2011,***16*,244-246
9. Verd, S.; Aguiló, S.; Kraemer,M.; Fernández,M.; Servera,C.; Colom,M. Palmer,P.; López-Sureda,M.; Juan,M.; Ripoll,J.; Juan Llobera,J. Past medical history: A comparison between children at the point of entry into the care system and children at home. *J Child Custody.* **2018**, *15*, 228-240,
10. Andropoulos, D.B. Pediatric normal laboratory values, in *Gregory's Pediatric Anesthesia*, eds. G. A. Gregory, G.A.; Andropoulos,D.B. 2012, 5th edition, Texas, Blackwell.
11. Chen, E.; Hanson, M.D.; Paterson, L.Q.; Griffin, M.J.; Walker, H.A.; Miller, G.E. Socioeconomic status and inflammatory processes in childhood asthma: the role of psychological stress. *J Allergy Clin Immunol*. **2006,***117,*1014-1020.

12. Raghavan, V.; Gunasekar, D.; Rao, K. R. Relevance of Haematologic Parameters in Obese Women with or without Metabolic Syndrome. *J Clin Diagn Res*. **2016,***10,*EC11-EC16.
13. Kaestner, T. L.; Santos, J. A. D.; Pazin, D. C.; Baena, C. P.; Olandoski, M.; Abreu, G. A.; Kuschnir, M. C. C.; Bloch, K. V.; Faria-Neto, J. R. Prevalence of Combined Lipid Abnormalities in Brazilian Adolescents and Its Association with Nutritional Status: Data from the Erica Study. *Glob Heart*. **2020**,*15*,23.
14. Licenziati, M. R.; Valerio, G.; Vetrani, I.; De Maria, G.; Liotta, F.; Radetti, G.
15. Altered Thyroid Function and Structure in Children and Adolescents Who Are Overweight and Obese: Reversal After Weight Loss. *J Clin Endocrinol Metab.* **2019**,*104*,2757-2765.
16. 15 Lertrit, A.; Chailurkit, L. O.; Ongphiphadhanakul, B.; Aekplakorn, W.; Sriphrapradang, C.
17. Thyroid function is associated with body mass index and fasting plasma glucose in Thai euthyroid population. *Diabetes Metab Syndr.* **2019**,*13*,468-473.
18. Vajro, P.; Fontanella, A.; Perna, C.; Orso, G.; Tedesco, M.; De Vincenzo, A.
19. Persistent hyperaminotransferasemia resolving after weight reduction in obese children. *J Pediatr.* **1994**,*125*,239-41.
20. Reinehr, T.; Schmidt, C.; de Sousa, G.; Andler, W. Association between leptin and transaminases: 1-year follow-up study in 180 overweight children. *Metabolism.* **2009**,*58*,497-503.
21. Burgert, T. S.; Taksali, S. E.; Dziura, J.; Goodman, T. R.; Yeckel, C. W.; Papademetris, X.; Constable, R. T.; Weiss, R.;Tamborlane, W. V.; Savoye, M.; Seyal, A. A.; Caprio, S.
22. Alanine aminotransferase levels and fatty liver in childhood obesity: associations with insulin resistance, adiponectin, and visceral fat. *J Clin Endocrinol Metab.* **2006**,*91*,4287-94.
23. Oh, R. C.; Hustead, T. R.; Ali, S. M.; Pantsari, M. W. Elevated Liver Transaminase Levels: Causes and Evaluation. *Am Fam Physician.* **2017**,*96*,09-715.
24. Ignjatovic, V.; Lai, C.; Summerhayes, R.; Mathesius, U.; Tawfilis, S.; Perugini, M. A.; Monagle, P. Age-related differences in plasma proteins: how plasma proteins change from neonates to adults. *PLoS One.* **2011**,*6*,e17213.
25. Adams, J. A.,;Starling, S. P.; Frasier, L. D.; Palusci, V. J.; Shapiro, R. A.; Finkel, M. A.; Botash, A. S. Diagnostic accuracy in child sexual abuse medical evaluation: role of experience, training, and expert case review. *Child Abuse Negl.* **2012**,*36*,383-92.
26. Starling, S.P.; Frasier, L.D.; Jarvis, K.; McDonald, A. Inter-rater reliability in child sexual abuse diagnosis among expert reviewers. *Child Abuse Negl.* **2013**,*37*,456-64.
27. Pavone, V.; Vescio, A.; Lucenti, L.; Amico, M.; Caldaci, A.; Pappalardo, X. G.; Parano, E.; Testa, G. Diagnostic Tools in the Detection of Physical Child Abuse: A Systematic Review. Children (Basel). **2022**,*9*,1257.