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Assessment of the Blood Lead Level in Children with Unexplained Failure to Thrive (FTT) admitted to Pediatrics Emergency Ward of Ghaem Hospital, Mashhad, Iran

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Abstract

Background

Lead is a strong and stable toxin, harmful especially to children, pregnant women, and the elderly. Nearly 27% of children aged under 5 years suffer from failure to thrive (FTT). Due to the probable harmful effects of lead poisoning on children's growth, in this study we aimed to assess the blood lead level in children with unexplained failure to thrive.

Materials and Methods

This analytic cross-sectional study was performed on 200 children under 2 years of age who were referred to Ghaem hospital, a referral hospital in Mashhad city-Iran. The participants were divided into two equal groups, one with unexplained FTT (group A), and children with normal weight (group B). Baseline characteristics were obtained by a research-made questionnaire. Blood samples were taken by the hospital nurses who were blind to the study groups. Blood lead level was measured by atomic absorption spectrophotometric method (Perkin Elmer 3030).

Results

The mean ± standard deviation (SD) of blood lead level in FTT group and control group were 7.3±3.32 µg/dL and 6.37±5.93 µg/dL, respectively. Blood lead level was significantly higher in FTT group than control group (P=0.001). Baseline Charactistics (such as hgender, parental educational level, gestational age, and socio-economic status of the family) were not significantly different between the two groups (P>0.05).

Conclusion

The results of our study revealed that blood lead level was higher in children with FTT. So Lead poisoning may be a potential cause of unexplained FTT. So, measuring blood lead level can be useful in diagnostic workup of patients with FTT.

Key Words: Blood, Children, Failure to Thrive, Lead.

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1- INTRODUCTION

Lead is a silver-gray heavy metal used in many industries and consumer products. It is a potent and stable poison with no known biological value in the human body. Lead have been used for many centuries and have several industrial applications. It can be found in almost everywhere and entrance of trace amounts of Lead into human body is rather inevitable, but in larger amounts, Lead can cause toxicity and clinical symptoms. The history of Lead poisoning and efforts to prevent this problem goes back to at least the 2nd century BC when the Romans, especially Lead workers and wine drinkers presented with symptoms of Lead toxicity (1, 2). Due to the growing general awareness of the Lead toxicity and its symptoms, preventive strategies have been developed and the incidence of clinically symptomatic Lead poisoning has declined in the recent decades. However, as the diagnostic methods for accurate detection of blood Lead level have developed, the attention has shifted towards the cases with sub-clinical Lead poisoning, especially in children that are the most vulnerable age group, to exposure Lead toxicity (3, 4).

Therefore, the normal blood lead level in children has been redefined to lower amounts several times by the world health organization (WHO), and Centers for disease control and prevention (CDC) (5). Failure to thrive (FTT), is defined as significantly lower rates of physical growth among infants or children, compared with their peers. In other words, FTT is diagnosed in children or infants with growth rates below the third or fifth percentiles or those with a growth decline from the 75th or higher percentiles to the 25th or lower percentiles in a short time (6). In most cases, complete history and physical examination will reveal the most likely etiologies and related management. However, in some cases, no underlying etiology is found in the patient by the primary assessments, and thus it is called non-organic or un-explained FTT, which implies that the primary etiology is external to the child's body. In such cases, specific and advanced assessments can help the physicians to find possible etiologies, an important one of which is elevated blood Lead level, which has been linked with impairments in synthesis of heme and neurotransmitters of central nervous system (7, 8). Therefore, this study aimed to determine the blood Lead level in patients with un-explained FTT compared the patients without FTT.

2- MATERIALS AND METHODS

This analytic cross-sectional study was performed on 200 children under 2 years of age referred to Pediatric Emergency Ward of Ghaem hospital, Teaching referral hospital, Mashhad University of Medical Sciences, Mashhad city, North East of Iran, from Dec 2014 till Dec 2015. We have two groups (100 patient in each group). Group A: children with un-explained FTT, and group B were age-matched patients without FTT. At first, all children who were referred to our center for any reason were screened for FTT by a complete history and physical examination. The diagnosis of FTT was made based on the guidelines of the WHO.

Therefore, any child with birth weight below 2,500 gr, with weight gain lower than 500 grams (gr) per month in the first 6 months, with no weight gain in 2 consecutive months between 6^{th} and 12^{th} months or in 3 consecutive months after the first year were considered as FTT. We also considered the children being two or more standard deviations (SDs) below the mean weight for their age and gender to have FTT (9, 10). The children who were diagnosed with FTT, were thoroughly evaluated and if the researchers found no known etiology for the patients' FTT, the children were enrolled in the A group (un-explained FTT). Children with normal

weight gain who had no FTT during the initial assessments were enrolled in the B group (control group). The severity of FTT was determined using weight for age, based on the Waterlow classification for children under the age of 10, as severe (< 70% of ideal weight for age), moderate (70% to 80% of ideal weight for age), and mild (80% to 90% of ideal weight for age) (11). All children with hereditary or congenital diseases that affect the somatic growth, those with a history of severe or chronic illnesses (>1 month), that have known negative effects on the child's growth (such as malabsorption, heart failure, mental retardation), those suffered from acute diseases that affect weight gain within a month before the study, were excluded from the study. We also excluded the ones whose parents did not give consent for participation in the study.

The parents of the children were given a brief explanation about the study and its objectives and then written consent were obtained from them. Baseline characteristics, medical history, physical examination data were gathered from all enrolled patients by the researchers using appropriate forms and questionnaires. After parents' consent, blood samples (1 mL), were obtained from all participants by hospital nurses. Blood samples were collected in heparinized Vacutainer™ tubes and sent for evaluation of blood Lead level. Sampling was done with the nurse of pediatric department from peripheral vessel; then the assessment of blood lead level was measured by the Atomic Absorption spectrophotometry of Perkin Elmer 3030 with HGA. All blood samples were sent to the central laboratory of Imam Reza hospital (Mashhad, Iran). In the laboratory a single technician handled measuring of all the study samples. The chemical reagents were Ammonium and Nitric acid. Plasma Lead concentrations were then determined using atomic absorption spectrophotometry (Perkin-Elmer 3030, Perkin-Elmer Corp, Norwalk, CT, USA), equipped with a HGA 500 graphite furnace atomizer and an automatic sampling attachment by standard 1 method. The severity of Lead toxicity was classified based on blood Lead level, as severe (≥70 µg/dL), moderate (45-69 µg/dL), and mild (≤44 µg/dL).

The Statistical Package for Social Sciences (SPSS; version 20.0 for Windows™) was used to analyze the data. The Kolmogorov–Smirnov test showed normal distribution for age (P>0.05), while blood Lead level data were non-normally distributed among the patients (P<0.004). Descriptive statistics (mean, frequency, and standard deviation [SD]), were determined for all variables. Laboratory data and demographic information were compared among groups, using Mann-Whitney U and Kruskal-Wallis H for non-normally distributed variables, and Chi-square test for categorical variables. Spearman test were also used to determine the correlation between the variables.

3- RESULTS

In the present study, out of the 200 studied patients, 121 (60.5%) were male, and 79 (39.5%) were female. However, no statistically significant difference was observed in blood Lead level between the male and female patients (P>0.05). There was no significant difference regarding the age, gender, and history of preterm birth, type of nutrition, parental educational status, maternal age, and socio-economic status in FTT and control groups **(Table1-5)**. In this study, mean age was 17 months in the FTT group and 16 months in control group. There was a negative correlation (r=-0.13) between the age of patients and their blood Lead level in the FTT group, while it was a positive correlation (r=0.13) for the patients in the control group. However, both correlations were not significant (P>0.05). Maternal age was

significantly and negatively correlated with the blood Lead level in the FTT group (r=-0.2; P=0.04). These variables also had a negative correlation in the control group, but it was not statistically significant (r=-0.05; P=0. 59). We found no significant relationship between the blood Lead level and type of nutrition (exclusive breastfeeding, no breastfeeding, or breastfeeding with complementary food) in children (P>0.05). There was no significant difference between the two groups regarding variables such as history of term or preterm birth, parental educational status, maternal age, and socio-economic status (income) of the family (P>0.05).

Considering FTT severity in the FTT group, 75% had mild FTT, 21% had moderate FTT, and 4% had severe FTT. Based on the results of Kruskal–Wallis test, the severity of FTT showed no significant relationship with the blood Lead level and the socio-economic status (income) of the family (P>0.05). Mean blood Lead levels were 7.3±3.32 µg/dL in FTT group, and 6.37±5.93 µg/dL in control group. As shown in **Table-6**, there was a statistically significant difference between the two groups regarding the blood Lead level (P=0.001). However, in terms of severity of Lead toxicity, there was a significant difference between the two groups; all FTT patients (100%) had mild toxicity, whereas one of the control patients (1%) showed moderate toxicity, and 99 (99%) had mild toxicity (P=0.001).

Table-1: Comparison of demographic data between FTT and control groups.

Groups	Gender	Number (percentage)	Blood lead level Mean (SD)	P-value
FTT, n=100	Female Male	45(45) 55(55)	7.2 (3.11) 7.38 (3.5)	0.97
Control, n=100 (without FTT)	Female Male	34(34) 66(66)	6.05(2.15) 6.53(7.15)	0.40

SD: Standard deviation.

Table-2: Comparison of gestational age between FTT and control groups.

Groups	Gestational age	Blood lead level Mean (SD)	P-Value
FTT, n=100	Term Preterm	7.22 (3.32) 7.9 (3.35)	0.53
Control, n=100 (without FTT)	Term Preterm	6.35 (6.11) 6.58 (2.83)	0.27

SD: Standard deviation.

Table-3: Comparison of education of parent between FTT and control groups.

Groups	Educational level of parent	Blood lead level(SD)	P-value
FTT, n=100	Under diploma Diploma & above diploma Licentiate	8.18 (4.34) 7.00 (2.79) 6.88 (2.96)	0.60
Control, n=100 (without FTT)	Under diploma Diploma & above diploma Licentiate	5.98 (4.16) 6.96 (7.78) 5.55 (2.17)	0.67

Table-4: Comparison of kind of nutrition & blood lead level between FTT and Control groups.

Groups	Status of nutrition	Blood lead level Mean (SD)	P-value
FTT, n=100	Milk of mother Completed nutrition Milk of mother & formula	5.06 (2.4) 7.36 (3.6) 7.50 (2.83)	0.29
Control, n=100 (without FTT)	Milk of mother Completed nutrition Milk of mother & formula	9.26 (8.7) 6.89 (8.26) 5.6 (2.27)	0.63

Table-5: Comparison of monthly revenue of family between FTT and Control groups.

Groups	Monthly revenue of family, (Rial)	P-value
FTT, n=100	4,950,000	0.08
Control, n=100 (without FTT)	6,830,000	0.08

Table-6: Comparison of blood Lead level between FTT and Control groups.

Variables	FTT group, n=100	Control (Without FTT), n=100
Mean (SD) BLL	7.2	6.37
Maximum BLL	23	56.3
P-value*	0.27	0.23

BLL: Blood Lead level; Values are reported in µg/dL; *Mann-Whitney test.

4- DISCUSSION

Childhood and infancy are pivotal periods for growth and development in the life of every human being and impaired growth in early childhood leads to manifold medical and psychological problems in later ages. Therefore, complete multidisciplinary evaluation, early diagnosis, and appropriate treatment of probable etiologies in children with unexplained FTT are crucial and will prevent adverse outcomes in further ages (8, 12). In this study we aimed to determine the blood Lead level in patients with un-explained FTT compared the patients without FTT. We found the blood Lead level to be significantly higher (P=0.001) in the children with un-explained FTT (group A), compared to those without FTT (group B). Similarly, in a study done by Bithoney on 45 patients with non-organic FTT that were compared with 45 age, race, and socio-economically matched controls, the results indicated significantly higher blood Lead levels in the FTT patients (P<0.001) (7). In several similar studies, blood Lead level has been reported to be relatively higher in children with specific diseases or medical conditions such as physical child abuse, lower body size, anemia, underweight, attention deficit hyperactivity disorder (ADHD), constipation, and malnutrition, compared to healthy comparison subjects (13-18). In the present study, we did not find any significant difference between male and female gender in both groups, regarding the blood Lead level. However, Gao et al. inconsistently found significantly higher blood Lead levels in symptomatic boys, compared the girls. They also found the blood Lead level to be higher in children with low parental education and those under 6 years of age, that were in contrast with our findings that indicated no significant relation between

children's age and blood Lead level (19). Our findings showed no statistically significant difference regarding the blood Lead level between children with history of term and preterm births. Andrews and colleagues in their review on prenatal lead exposure, indicated that despite prenatal lead exposure was unlikely to induce premature rupture of membranes, it appeared to be able to increase the risk of preterm delivery. However, the results were not statistically significant, which is in line with our findings (20). We did not find any significant difference between the children with different types of nutrition (exclusive breastfeeding, no breastfeeding, or breastfeeding with complementary food), in regard with the blood lead level. In contrast, Goyer and Rhyne found the nutritional status of children to be significantly related to their blood Lead level (21). In the present study, we found no statistically significant relation between the socio-economic status of the families and blood Lead level in their children that is in line with the findings of Brooks-Gunn and Duncan. In their review on the effects of poverty on children, Brooks-Gunn and Duncan found no significant relation between blood Lead level in children and the economic issues of their families (22).

Lead poisoning may contribute to some deleterious effect on patients, its role in anemia, immune imbalance and delayed skeletal development have been reported in different studies (24). Although many aspects of lead poisoning has been studied in the literature, up to now, only few studies have measured blood lead level and evaluated the rate of lead poisoning in children with FTT, especially un-explained FTT. Therefore, this study is the first of its kind in Iran and among the very few studies worldwide to evaluate lead poisoning in children suffering from un-explained FTT.

4-1. Limitations of the study

In this study, we had some limitations, one of which was that we did not obtain information about environments that the patients live in, thus we could not assess the role of environmental exposures on the blood Lead level of the patients. May be if we collected samples from different cities with different environmental Lead exposure levels, we could draw a better conclusion. In addition, due to the cross-sectional design of the study, it was not possible to analyze the cause and effect relations and to evaluate whether the blood Lead level was effective in development of FTT or not. Moreover, we did not assess the Lead concentration of blood and breast-milk in breastfeeding mothers, which has been reported to be significantly effective on the children's blood Lead level (23). Finally yet importantly, a larger sample size and a second confirmatory assessment of blood lead level in the patients would have helped us to make the results stronger and more significant.

5- CONCLUSION

In this study, we observed high blood lead level in children with unexplained FTT comparing normal weight matched group. Measuring blood lead level as a potential cause of FTT and planning preventive strategies in order to reduce environmental exposures to Lead, especially in children may be important in patients with FTT. Although before generalizing the results and modifying the diagnostic protocols of FTT, additional studies in different population may be necessary.

6- CONFLICT OF INTEREST: None.

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