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SERUM LEAD LEVEL IN A SAMPLE OF EGYPTIAN CHILDREN WITH SPECIFIC LEARNING DISABILITIES: CROSS-SECTIONAL STUDY

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Abstract

Background: learning disability can be defined as a condition that impairs the person's capacity for thought and memory. Specific learning disabilities (SLD) can be divided broadly into three categories which are dyslexia, dysgraphia, and dyscalculia. Damietta government is an industrial area which makes lead exposure more frequent among the children. The nervous system is the most sensitive system adversely impacted by lead. In this work we have studied the relation between serum lead level, specific learning disabilities (SLD) and psychiatric co-morbidity in an Egyptian student's sample.

Results the study included 170 students. Significant relation between serum lead level and specific learning disabilities was found in the studied sample. However, in regard to serum lead level and Psychiatric co morbidity, no significant relationship was detected.

Conclusions: Based on the results, after analysis for the relationship between SLD, psychiatric co morbidities and serum lead level, the detection of SLD at a blood lead level of 0.150 ug was only 50.8% specific and 61.0% sensitive among the studied sample. Longitudinal research will be needed to see long term effect of lead exposure.

Keywords: Learning disabilities, Psychiatric co morbidity, serum lead level, children.

BACKGROUND

Specific learning disabilities (SLDs) encompass a range of disorders that impair various cognitive and academic abilities. These conditions, characterized by deficits in fundamental psychological processes and affect specific set of skills including reading, writing, and mathematics. SLDs are often identified using the aptitude-achievement discrepancy model, where academic performance in specific domains is significantly below what is expected based on general intelligence. For a diagnosis, children typically have average or above-average IQ scores, but their academic achievement scores fall two or more standard deviations below expectations. A diagnosis can only be made a after exclusion of intellectual disability, visual or auditory impairments, insufficient education, and psychosocial trauma [1 2]

The etiology of SLDs is believed to be rooted in biological factors, with research identifying cognitive deficits in auditory processing, phonological coding, and syntactic processing instead contributed to reading problems rather than visual processing impairments. However, it remains unclear whether these deficits are causative, consequential, or correlated with SLDs [3]

Lead (Pb) is a xenobiotic metal, has effect on cellular development, proliferation, or signaling. Years of study into the toxicity of Pb have revealed that it is a serious neurotoxin, especially when the nervous system is developing. More than any other body system, the neurological system is highly prone to be affected by Pb.[4]

It is estimated globally that learning disability has a prevalence of 5% among school-aged children, though some estimates suggest the prevalence may be as high as 15-20% [5]. In Egypt, LDs are reportedly present in 16.5% of children, with little awareness of their causes and risk factors. Furthermore, psychiatric comorbidities often coexist with SLDs, compounding their impact on children's development [6].

We aim to examine in this study the relationship between specific learning disabilities (SLDs), serum lead levels, and psychiatric comorbidities in a sample of Egyptian students residing in the Damietta Governorate, an industrial region where school-aged children may face increased exposure to lead. By investigating these associations, the research seeks to better understand how environmental and neurodevelopmental factors influence the development of learning disabilities and their broader implications on children's health and academic performance.

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METHODS

Study Design and Duration:
This is a cross-sectional study with analytic component that was carried out across one academic year from December 2021 till December 2022**.** Cluster random sample was retrieved. From each school, two different classes from the fourth grade and two classes from the fifth grade were involved. A random draw for the classes of students in the study was done to ensure no bias in selection.

Study questionnaires
1.**Socio-Demographic and clinical data :**To gather data on the demographics of the study participants, in-person interviews were conducted with their parents. Subsequently a **Socioeconomic status scale (SES) for health research in Egypt was applied**. It assesses the socioeconomic status in 7 areas for a combined score of 84 [7].
2.Screening for Psychiatric Morbidity
The Semi-structured Clinical Interview for Children and Adolescents (SCICA) was conducted. It uses open-ended questions to help subjects talk and behave in a free way that revealed their thoughts, interests, feelings, concerns and their interaction style as well in different situations. Following the interview, the interviewer graded the SCICA scoring forms' 107 self-report items and 117 observation items. A profile of experimentally derived syndrome scales is created by combining the items from the two score formats. Anxious, withdrawn, attention-deficit, weird, and resistant are among the symptoms on the observation-based syndrome scales. On the self-report scale, there are items for anxious depression, family issues, and aggressive conduct. Two additional broadband internalizing and externalizing scores are also produced by the SCICA. [8] Amr et al. (2009) translated the SCICA into Arabic, and it had convergent validity and test-retest reliability comparable to the original. We exclusively used the observational form in this investigation.[9]
Clinical Psychiatric Interview was then conducted to determine whether 13 common childhood mental disorders were present, using the Diagnostic and Statistical Manual of Mental Disorders, DSM-5-Criteria. Its diagnostic process is comprised of closed-ended, organized inquiries.
3. Screening for reading disability using (Reading disability test (RDT) of Gilgil) With strong reliability and validity scores. After computing the averages and standard deviations in regards to the student performance in each of the relevant phases, the result was calculated. The fifth-grade cutoff score is 57, and the fourth-grade cutoff score is 49. [10]
4. The writing and mathematical part of Zayat Assessment Battery for Learning Disabilities: we used only the part of mathematical and writing as they are the relevant parts to our study. The battery assessment is based upon the observation and rating of a teacher, or parent of the frequency and permanence of certain characteristics that differentiate those with learning disabilities. The assessment should rely on observations in different settings. The cut off score is 20 for both writing and mathematical part, any score above that number indicate having writing or mathematical disability of varying degree [11]
5. Raven Progressive Matrices (RPM):
It is a nonverbal test that encompass one missing component. The Progressive Matrices obtained data was converted to percentiles to calculate the final result using the scale handbook [12].
6. Blood serum lead level: blood samples were collected by venipuncture technique into Vacutainer tubes from children then digested then the lead level was analysand by (Inductively coupled plasmas) ICP Analysis Method.
Centers for Disease Control and Prevention (CDC) announce **Blood PB Level (µg/dL) Health Risk / Interpretation to be as follow** [13]:

Blood Lead Level (µg/dL)	Health Risk / Interpretation
0 – 1	Ideal — minimal risk
1 – 3.4	Low level — potential subtle effects
≥ 3.5	CDC reference level — action recommended
≥ 5	Elevated — associated with developmental and behavioral issues
≥ 10	High risk — significant neurotoxic effects
≥ 45	Requires medical treatment (chelation)

Sampling and sample size calculation
Participants:
Sample size calculation was figured on the prevalence of dyslexia 11.3% (which is a specific learning disability) retrieved from previous research [14], A whole of 190 school children, both males and females, were the initial sample. However, only 170 students fulfilled the inclusion criteria, which were: Students in the 4th and 5th primary grades of

both genders, with services available for compensating specific learning difficulties with no sensory disabilities (e.g., hearing or visual impairments), intellectual developmental delays, neurological or motor disorders, or developmental disorders. Written informed consent was obtained from all participants' parents. All 190 students have done Raven's Coloured Progressive Matrices and 9 children below the average IQ score were excluded. Another 3 students had sensory impairment were excluded and 8 students were also excluded as blood sampling was not feasible due to intense fear of needles. The final sample was 170 students.

Then the students who had a possible SLD according to Reading disability test (RDT) of Gilgil and the writing and mathematical part of Zayat Assessment Battery for Learning Disabilities were labelled as the ones who have SLD and the cut off point for each scale are shown in the instrument section. The sample was recruited from governmental educational system in Damietta which included (Khaled Ibn Elwaleed public school for primary education, Zed Ibn Haartha experimental school for primary education, El khlfaa El Rashden Azhari for primary education).

Statistical analysis

To analyze the date, SPSS software, version 25 was utilized. Chicago, Illinois: SPSS Inc. The median and mean ± were utilized to characterize quantitative data in regard to the non-normally distributed data. T test was utilized for the properly distributed data. For the comparison of the qualitative data between groups, Monte Carlo, Fischer exact, and chi-squared tests were employed. Enter approach and binary logistic regression was also employed to examine for the impact while combining more than two independent variables on a dichotomous outcome.

RESULTS

Table (1): Comparison of Sociodemographic and Clinical Characteristics by SLD

Variable	SLD Present (n=65)	SLD Absent (n=105)	p-value
Age group, number (10/11years)	41/24	55/50	0.172
Sex group, number (Boys/Girls)	36/29	54/51	0.616
Positive Family History of psychiatric disorders (%)	20 (30.8%)	16 (15.2%)	0.016*
SES Score (Mean ±SD)	59.12±9.20	61.0±8.98	0.191
IQ (RPM Score)	25.17±3.52	26.65±3.19	0.005*
Reading Disability Test	53.61±14.31	62.51±11.77	<0.001*
Writing Disability Test	36 (5–77)	14 (5–77)	<0.001*
Math Disability Test	36 (2–77)	16 (2–75)	0.005*
Psychiatric Comorbidity (%)	22 (33.8%)	14 (13.3%)	0.001*
Values are presented as mean ± SD or median (range) as appropriate, SLD stands for specific learning disability ***= statistically significant at p < 0.05.**			

Table (1) when it comes to the sociodemographic factors and clinical presentation, there a significant statistical difference between the children with SLD and the children without SLD regarding RPM, SLD test and psychiatric co morbidity.

Table (2): psychiatric co-morbidities and speech comorbidities among the studied cases:

	N=170	%

Psychiatric comorbidities	N=36	
Social phobia	3	8.3
PTSD	2	5.6
Oppositional defiant disorder	4	11.1
Needle phobia	2	5.6
Intermittent explosive disorder	1	2.8
Generalized anxiety disorder	11	30.6
Depression	3	8.3
Conduct	2	5.6
ADHD	8	22.2
Speech abnormalities		
Absent	166	97.6
Stuttering	4	2.4

Table (2) showed that the most prevalent psychiatric co morbidity was generalized anxiety and about 2.4% of the students showed stuttering.

Table (3): Serum Lead Level by SLD Status

Group	Lead Level (µg/dL) mean ± SD	p-value
Children without SLD	0.0–10.65	0.135
Children with SLD	0.3–10.65	

Table (3) showed the relation between lead level range and SLD status, the range of lead level in subjects with no learning disability was (0-10.65) Ug while in subjects with learning disability was (0.3-10.65) Ug. No significant statistical value was found in that regard between children with and without SLD.

Table (4): Predictors of Learning Disability (Logistic Regression Analysis) Among the Studied sample.

Variable	B Coefficient	p-value	Odds Ratio (95% CI)
Family history of psychiatric disorders	0.598	0.143	1.82(0.816-4.05)
IQ test (Raven Progressive Matrices)	-0.003	0.957	0.997(0.883-1.13)
Reading disability test	-0.036	0.035*	0.964 (0.932-0.997)
Writing disability test	0.018	0.054	1.02 (1.0-1.04)
Psychiatric comorbidities	1.02	0.012*	2.78(1.25-6.17)
(r) = reference category; Overall % predicted = 69.4%; * = statistically significant at p < 0.05.			

According to predictors of learning difficulties among studied cases, **table 4** showed that the presence of psychiatric co morbidity were predicators for developing a SLD.

Table (5): Validity of Blood Lead Levels in Differentiating students with Learning Disability

Parameter	Value
AUC (95% CI)	0.562 (0.472-0.651)
p-value	0.176
Cut-off point (µg)	0.150
Sensitivity (%)	50.8
Specificity (%)	61.0
AUC = Area under curve	

Table (5) revealed that detecting SLD at a blood lead level of 0.150 ug was only 50.8% specific and 61.0% sensitive.

TABLE (6): CORRELATION BETWEEN BLOOD LEAD LEVEL AND ACADEMIC/COGNITIVE TESTS AMONG STUDIED SAMPLE.

Test	Correlation Coefficient ®	p-value
Writing disability test	0.314	<0.001*
Math disability test	0.200	0.009*
Raven Progressive Matrices (RPM) tests	-0.254	0.001*
Reading disability test	-0.457	<0.001*
Socioeconomic status score	-0.09	0.242
r = Spearman correlation coefficient; * = statistically significant at p < 0.05.		

Table (6) revealed that among the sample analyzed, there was a statistically significant correlation between lead level and the results of tests for writing, math, and reading disabilities as well as Raven Progressive Matrices (RPM) test score.

Table (7) Relationship between psychiatric comorbidities and lead level.

Psychiatric comorbidities	Lead	Test of significance
Social Phobia **PTSD** **Oppositional Defiant Disorder** **Needle Phobia** **Intermittent explosive Disorder** **Generalized Anxiety Disorder** **Depression** **Conduct** **ADHD**	0.6(0-2.15) 4.72(3.45-6) 0.6(0.0-2.25) 4.5(0-9) 0(0-0) 1.05(0-2.85) 0(0-3.15) 0(0-0) 1.5(0-3.15)	 Kw=8.95 P=0.346
Negative family history **Positive family history**	0(0-10.65) 0.825(0-9)	Z=1.36 P=0.174

Table (7) demonstrate that no significant relationship was found between psychiatric co morbidities and lead level in our studied sample.

Table (8): Observational Scores of the SCICA in Students with and without Learning Disability.

	SCICA score		P Value
	With SLD N=106	Without SLDN=65	
Anxious	52.9±5.6	62.9±6.2	0.001*
Withdrawn	54.4±7.1	55.98±6.5	0.147
Attention	41.8±5.1	43.5±6.9	0.07
Strange	45.3±6.9	60.5±5.7	0.001*
Resistant	52.6±11.65	63.4±10.92	0.001*
Total observation	49.6±10.8	61.69±10.25	0.001*

Note: SCICA = Semi-structured Clinical Interview for Children and Adolescents

Table (8) describe the observational scores of the SCICA in both children with and without SLD. All subscales showed lower mean scores in children with SLD, with the strange, anxiety, and resistance subscales showing significant difference among both groups.

DISCUSSION

The majority of the tested samples were male, according to the demographic information. Additionally, nearly 21% (N=36) of them demonstrated a family history of psychiatric diseases, with anxiety disorders being the most prevalent (47.2%).

El Sheikh and his colleagues have shown in a similar vein that 11.3% of the Egyptian students attending primary school had dyslexia and that boys were three times higher than girls. In 57.8% of the sample, comorbidity with other mental illnesses was discovered. 33% of patients had attention deficit hyperactivity disorder (ADHD), 21.6% had anxiety, and 16.2% had depression. [14]

In our study we found that the total incidence of SLD was 38.2 among the studied sample. One factor that might explain the high prevalence is the objective nature of the writing and mathematical part of Zayat Assessment Battery for Learning Disabilities which relays on observation from the parents and the teachers.

The prevalence of SLD for children in schools across all languages and cultures, according to the American Psychiatric Association, ranges from 5 to 15%. [15]. Ismail and his colleagues assessed learning disabilities (LDs) prevalence in a group of Egyptian children aged 6 to 12 while taking into account the associated sociodemographic risk variables. The primary conclusions that could be drawn from this study were that 16.5% of the tested sample had LDs [5].

A study by **Karande and his colleagues** estimated the prevalence of SLD between students in a South Indian city's primary school to be 11.2% [16]and research by the same effect was found by **Fluss and his associates** in a sample of French students from elementary schools [17]. Both studies found that the incidence rate of SLD among these students was 12%.

About 4.9% of children in Canada, ages 6 to 15, were found to have a learning disability; the frequency ranged by age, from 1.6% for 6-year-old to 7.2% for 10-year-old Dyslexia, which impacts a wide range of reading and language skills, is the most prevalent LD, affecting 80% of those with LDs [18].

With regard to lead concentration, the present study showed that the mean result for the Pb concentration in the obtained blood samples was 1.42±2.41 Ug/dl. **Evens and his colleagues** found that the average level of the cases they analyzed was 4.81± 2.22. Additionally, **Reuben and his colleagues** have shown that 579 (55.6%), of the 1037 original study children, were examined for lead exposure at the age of 11 (of whom 311 (53.7%) were male) and Lead levels in blood were 11.08 (4.96) g/dL on average (SD) [19].

Data from 5688 public schools were examined by **Cradock and his colleagues**. The schools distributed across seven different states and all of these states had lead contamination over the state action threshold. The number of samples differs for every school. Between 13% and 81% of schools reported sample lead levels higher than 5 ppb. Only four states went over 20%. [20]

The current investigation showed that a blood lead level of 0.150 ug was only 50.8% specific and 61.0% sensitive in detecting SLD, raising questions about the efficacy of lead in separating people with learning impairments.

This was consistent with previous research that showed children whom blood lead levels were between the 50th and 100th percentiles were meaningfully more likely to have a learning disability their peers who were between the 0th and 50th percentiles as a result, it was imaginable to determine from the number of weighted people studied that 1,025,695 people in the US who were born between 1989 and 1998 had been diagnosed with Learning disability linked to elevated blood Lead levels [21]. Additionally, since 3,911,498 weighted individuals with LDs were evaluated, this indicates that 26.2% of all Learning Disabilities were linked to higher blood Lead levels. As a result, various environmental and/or genetic factors account for the bulk of LDs .[21]

It seems reasonable that a study discovered that there were more men than women with LDs since Lead damages brain tissue by increasing inflammation, apoptosis and oxidative stress in the brain. According to studies, women are more adept at controlling excessive brain inflammation and cell death [22 23]. This could explain why in our work male children with SLD was slightly higher than female with SLD.

Other research has found that lead exposure has a higher impact on boys. For instance, **Jedrychowski and his associates** used cord blood Lead level (BLL) to evaluate the cumulative Lead exposure during pregnancy in infants [24]. To evaluate cognitive deficiencies, they employed the Mental Development Index (MDI). According to the research's findings, children's lead poisoning has no upper limit, and boys aged three are more vulnerable to prenatal very-little lead toxicity than girls [25].

In our work the after Clinical assessment and analyzing the score of all the scales used for SLD, we found that the most common disability, with a 29.4 incidence rate, was reading impairment. Additionally, among the cases examined, the current study revealed a significant association between lead level and the results of writing, mathematics, and reading disability tests as well as IQ scores.

Accordingly, **Evens and his coworkers** have shown that the chance of failing in both reading and math increased by one third more than the average for every 5 g/dL increase in blood Pb levels. Lead had a nonlinear influence on reading, with higher failure rates at lower blood lead levels. They determined that 14.8% with failure in math and 13% with failure in reading in Chicago kids are direct correlation of exposure to blood lead level that ranged between 5 to 9 g/dL [26].

Similarly, **Zhang and his coworkers** have shown that low academic achievement in grades three, five, and eight was closely related with high lead levels in blood before age six years. After adjusting for potential confounders, those with lead levels larger than ten µg/dL had more than double the likelihood of scoring below competent as those with blood lead levels less than one µg/dL. So, after controlling for significant possible confounders, they came to the conclusion that lead exposure early on, had a negative impact on academic achievement in school. [27].

Similar to this, **Reuben and his colleagues** demonstrated that the 1.34-point increase in manifestation of thought disorder symptoms and internalizing disorder for each 5-g/dL increase in children's blood Pb levels. Furthermore, neuroticism rose by 0.10 standard deviations and conscientiousness fell by 0.14 standard deviations for every 5-g/dL increase in children's blood lead levels [19].

In our work, there was no significant relationship between psychiatric comorbidities and lead level. However, in a study conducted in Sanandaj, Iran, on workers in a variety of occupations, such as welding, painting, gas station workers, and non-exposed individuals. Blood lead levels were examined, a psychiatric disorders questionnaire (-90Checklist Symptom 90-Scl) was used to evaluate the psychiatric disorders, and 64 individuals were deemed to be the non-exposed group and 124 were chosen as the exposed group. Those who were not lead exposed had the lowest score of blood levels, with an average of 14.7500 mu g/dl, whereas welding employees had the highest, with an average of 63.3500 mu g/dl. Additionally, welding employees had the lowest quality of life and the highest psychiatric problems, while non-exposed individuals had the highest quality of life and the lowest psychiatric illnesses [28]. This discrepancy with our study might be due to prolonged exposure and higher blood lead level among these workers compared to our study population.

McGee et al. concluded that males with reading disabilities were almost three-fold more prone to manifest an externalizing disorder than their peers [29]. The main cause of this was the disproportionately high percentage of kids with LD in spelling (without ADHD, 6.1%; ADHD, 30.2%) and written expression (without ADHD, 27.3%; ADHD, 65.1%). Compared to the 33 children without ADHD (39.4%), the 86 children with ADHD (69.8%) had a higher prevalence of one or more forms of LD.

In contrary, **Puttaswamy A**, reported that while learning impairments in reading (reading comprehension or basic reading) and arithmetic (numerical operations) were extra common in kids with ADHD than in kids without the same disorder, the differences in frequency was not statistically significant [30].

In regard to the observational scores that result of the SCICA analysis's result among students with learning disability and those without learning disability in our study, all subscales showed significant lower mean scores in children with SLD, with statistical significance between both groups regarding the anxiety, strange, and resistance subscales.

This result is slightly different from the result of study done **Amr et al., 2009**, they found non-significant relation between two groups of their study regarding the following (withdrawn, anxious /depressed, internalizing, externalizing) respectively, while significant statistical difference was reported between the two groups regarding (anxious, family problems, aggressive behavior, strange, resistant, attention) respectively [9]. The difference between both studies may be due to difference in type of participants in both studies.

Limitations:

The current study's primary limitation was that it was cross-sectional, so it cannot establish causality between lead exposure and SLDs only associations. Serum blood lead was measured at a single timepoint, which may not accurately reflect long-term exposure and is susceptible to handling errors. Additionally, it conducted in a single governorate in a single country without taking into account lead-mediated racial changes which may limit generalizability. Because Blood lead level is primarily impacted by environmental factors like the presence of factories and water pollution, future studies must be conducted while taking these significant factors into account. Finally, other neurotoxicants common in industrial areas (e.g., manganese, mercury, air pollution) were not considered, so attributing observed effects solely to lead should be done cautiously.

CONCLUSIONS

This study highlights the association between specific learning disabilities (SLDs), serum lead levels and psychiatric comorbidities among children attending primary school in Damietta, Egypt. Although the sensitivity and specificity of serum lead levels as a standalone predictor of SLD were modest, higher lead exposure had a significant statistical correlation with poorer performance on reading, writing, and mathematical assessments, as well as lower IQ scores. This shed some light on the influence of toxins in environment on children's cognition and psychological development. Given the cross-sectional design, causality cannot be established. In conclusion, early screening for lead exposure particularly in industrial regions, should be prioritized in public mental health and educational policies.

Abbreviations
DSM-5: Diagnostic and Statistical Manual of Mental Disorders (Fifth edition)
SCICA: Semi-structured Clinical Interview for Children and Adolescents
IRB: Institutional review board
PTSD: Post traumatic stress disorder
ADHD: Attention Deficit and Hyperactivity Disorder
SLD: Specific Learning Disability
RPM: Raven Progressive Matrices
SPSS: Statistical Package for the Social Sciences
WHO: World Health Organization
ICP: Inductively coupled plasmas

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Contributions
M. R. E. conducted the interview for the children and their parent and gathered the data. E. A. E. contributed in writing the manuscript. M. A. A. contributed in writing the manuscript. Editing and revising the manuscript was conducted by I. M. I. and M. A. E. The finalized manuscript was read and approved by all authors.

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Declarations
Ethical approval: The ethical committee of the Mansoura faculty of medicine approved the study (IRB no. MD.21.09.531). Informed consent was obtained in a written format from all the parents of the children. Data of the patient were kept confidential.

Consent for publication
Consent obtained from all the children's parents prior to submission for publication.

Competing interests
There are no conflicting interests, according to the authors.

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