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Blood Lead Concentrations and The Neuropsychology Scores of Pregnant Women in Klang Valley, Malaysia

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Abstract

Pregnant women with high blood lead posed high risk to their fetus as placental transfer can occurs to the fetus. The objective of this study was to identify the relationship between blood lead and the neuropsychological score of women who were in their 3rd trimester of pregnancy. These respondents were undergoing a routine antenatal checkup at a teaching hospital located in Klang Valley areas. Blood lead concentrations were analyzed using graphite furnace Atomic Absorption Spectrophotometer (AAS). The neuropsychological scores were measured with WHO Neurobehavioral Core Test battery (NCTB). The test consists of 7 items, which made up of the Digit Symbol, Trail Making, Digit Span, Benton Visual Retention Test, Pursuit Aiming, Santa Ana Manual Dexterity, Reaction Time and Movement Time tests. The mean blood lead was 7.78±4.77 µg/dL. The mean score for the total NCTB test was 50.00±5.24. Statistical analysis showed blood lead concentrations were inversely correlated with the total NCTB score ($r = -0.462$, $p \leq 0.01$). The correlation was about 21.3%. The General Linear Model (GLM) showed that age ($\beta = -0.15$, $p = 0.017$), weight ($\beta = 2.67$, $p = 0.05$) and height ($\beta = -1.97$, $p = 0.05$) also influence the total neuropsychological scores. In conclusion, blood lead reduces the total neuropsychological scores. The scores for each of the 7 items were inversely and significantly correlated with blood lead concentrations except for the Trail Making and Santa Ana Manual Dexterity tests.

Keywords

Neuropsychological scores, blood lead concentrations, pregnant mothers

INTRODUCTION

Lead could be produced by human activities such as industrial, mining and agricultural activities that can spread by air, water and soil (1). Lead route of entry to human body through the inhalation, ingestion and skin contact. Lead has no function in human body. Previous study suggested lead has a negative effect on human health even though at very low level. Lead is a neurotoxin and its toxicity affect the function of the central nervous system and peripheral nerve. For adults, the main effects are peripheral neuropathy whereby the impulse conduction in the nerve is slowed down. Peripheral neuropathies influence the motor and sensory nerve. The effects are the wrist and the ankle drop that are the result of the defect in the radial and peroneal nerves (1).

Pregnant woman is at very high risk to the lead toxicity because pregnant mothers need high level of nutrient such as calcium as well as iron to support the growth and the development of the fetus. Lead could replace the function of calcium and iron. Tests on the biochemical and physiological process found that the concentration of calcium and iron in the blood are inversely proportional to the lead concentrations (2).

Study shows blood lead levels (BBLs) in pregnant women at 20.8 µg/dL can cause maternal disorders, when BLLs reaches 2.57 µg/dL, it can cause stress and fatigue levels in pregnant women (4). BLLs <5 µg/dL may cause pregnant women to have pre–eclampsia and endanger the mother's kidney, while BLLs <10 µg/dL can increase blood pressure or hypertension (4). Another research done by Bayat et al, 2016 showed there was an increase in systolic blood pressure (0.014 mmHg) and diastolic (0.013 mmHg) following the increase of 1 µg/dL of BLLs ($p = 0.04$) (5).

This study aims to investigate the association of BLLs with neuropsychology of pregnant women in Klang Valley, Malaysia. Klang Valley area was an ex-mining erea in Peninsular Malaysia. Active mining activity was in 1950-1970. The residue of lead and others heavy metal was still high in air, water and soil. The Neurobehavioral Core Test battery (NCTB) can detect early signs of disturbance or failure on the functions of nervous system. WHO was introduced NCTB identifying the nervous dysfunction among workers who are working with the neurotoxin chemicals (3).

MATERIALS AND METHODS

The study population is women in their 3rd trimester of pregnancy who reside in the Klang Valley areas. These pregnant women were attending their routine antenatal checkup at a hospital in Kuala Lumpur. Total 202 respondents were selected through purposive sampling based on specific criteria, that she must be Malaysian citizen, in the 3rd trimester pregnancy and have signed consent to participate. Their pregnancies were categorized as “high–risk” because they were referral cases from private or government clinics within the areas. These women were either in their 1st or 5th pregnancies, had hypertension, diabetes, anemia or a history of previous delivery complication.

Questionnaire interviews were carried out to collect information on the demographic as well as socioeconomic background and their health status. The questionnaire consists of the questions on their age, ethnicity, number of children, educational level, occupation and areas of residential. While the questions on health status include of number of deliveries, medical history, smoking habit, alcohol intake and medication during pregnancy.

Blood Sampling and Analysis

Venous blood was sampled during or after the 28 weeks of pregnancy. Five (5) ml of the blood samples were put into a special vacuum container tube, which contained heparin (anticoagulant). All sample of blood lead were analyzed using Graphite Furnace Atomic Absorption Spectrophotometer model HITACHI Z5700 with polarized Zeeman. Blood sample were diluted with matrix modifier solution in a ratio of 1:5. The modified matrix solution also acts as antifreeze agent during storage. The modified matrix solution consists of 10 mL Triton–X, 10% 0.3 g ethylene diamine tetra acetic acid (EDTA) and 5 g ammonium dehydrogenate phosphate in 1–liter deionizer distilled water. Lypocheck sample were used as a reference sample for quality control procedure during the analysis.

Neuropsychological Assessment

A neuropsychological test conducted in this study were Neuropsychological Core Test Battery (NCTB) and it is commonly used by WHO (3). It was an instrument used to detect early nervous systems failure because of the exposure of neurotoxin agents. This instrument is very sensitive and can detect early sign of nerve disturbance at a very low level of exposure. It consists of the Benton Visual Retention, Digit Span, Digit Symbol, Pursuit Aiming, Reaction Time, Santa Ana Manual Dexterity and Profile of Mood States (POMS) tests. However, the POMS test was not be conducted in this study, instead it was replaced by two more tests, Movement Time and Trail Making tests. The description and functional domain of the tests are shown in Table 1.

Standard Score Calculation

The raw score obtained from the neurobehavioral tests, was transformed into standard scores. From these transformed data or standard scores, the mean value is 50 and the standard deviation is 10. The calculation for the standard score is shown:

Standard score = [(raw data – mean) / standard deviation] x 10 + 50.

Table 1. Descriptions of Neuropsychological (NCTB) Tests

Test	Functional domain tested	Description
Reaction/Movement time	Attention/Response & movement speed	It measures how fast a person reacts/moves. It requires sustained attention by the subject.
Digit span	Auditory memory	It is a test of immediate (short–term) auditory memory that requires focused attention.
Santa Ana Manual Dexterity	Manual dexterity	It requires rapid eye–hand coordination movements.
Digit symbol	Perceptual–motor speed	It is a test of perceptual motor speed that also requires learning of associations.
Benton visual retention	Visual perception/memory	It is a short–term visual memory that requires focused attention. It also measures the ability to organize geometrical patterns in space and memorize them.
Pursuit aiming	Motor steadiness	It measures the ability to make quick and accurate movements with the hand.
Trail making	Motor tracking	It measures visual motor tracking and visual scanning. It requires an attention.

Source: WHO. 1983. Operational Guide for The WHO Neurobehavioral Core Test Battery. World Health Organization, Geneva. 15 Februari (14).

Ethical Clearance

This research was approved by the Research Ethics Committee of Hospital Universiti Kebangsaan Malaysia (UKM/EC711002105465-1). Involvement of respondents is based on a written agreement with filling a consent form. Respondents may withdraw at any time if they do not agree or are not satisfied with any study procedures.

RESULTS

Table 2 shows the demography and socioeconomic background information of the respondents. The mean age for mothers was 29.6 years old and their mean gestation period was 31.6 weeks. The ethnic and religious distributions of the respondents are shown in Table 2. The Malays made up 58.4 % of the respondents. About 35.6% respondents are full time housewives; while others work as general worker, operate a business, self–employed or part–time wage earner. The average household income is RM 2884.7 (Table 2). The mean blood lead level was 7.78 with standard deviation of 4.77 µg/dL.

Figure 1 shows the data distribution of blood lead for the respondents. Kolmogorov–Smirnov Normality Test shows that the distribution was normal ($p > 0.05$).

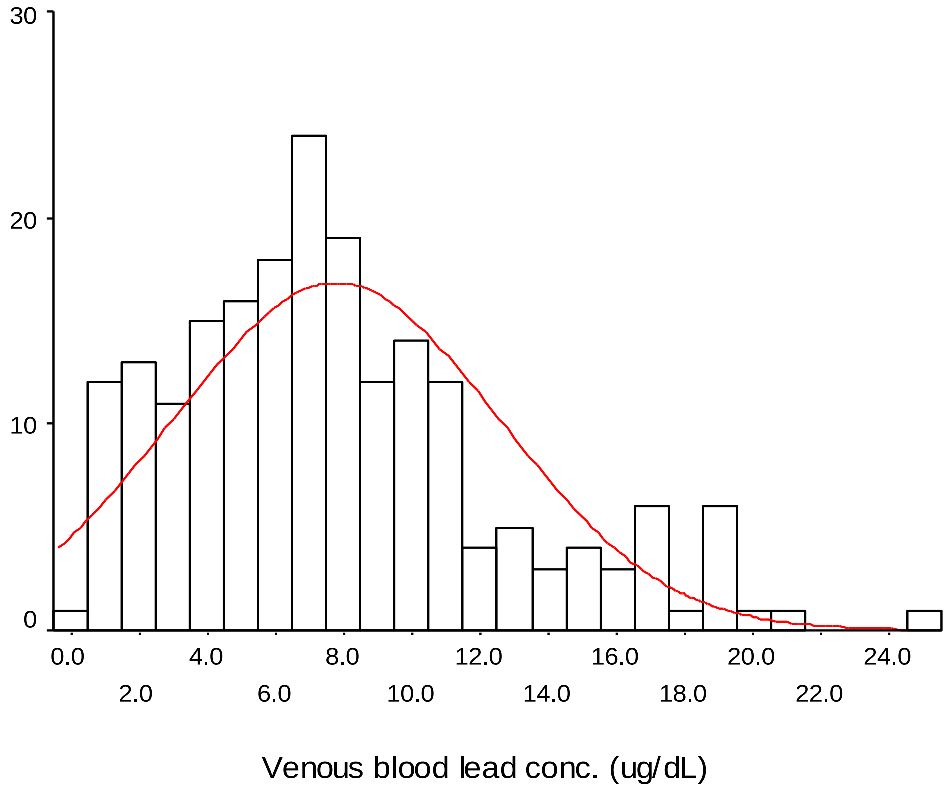

Fig 1. Distributions of Blood Lead Concentrations (µg/dL)

Table 2. Respondents' Demographic and Socioeconomic Background

Variable	Range	Mean	Std. Dev.
Mother age (Year)	19 – 44	29.6	5.57
Mother Education (Year)	6 – 19	12.1	2.08
Father's education (Year)	6 – 22	12.8	2.64
Total Household Income (RM)	750 – 8500	2884.7	1383.98
Mother's height (m)	1.43 – 1.72	1.57	7.12
Mother's weight (kg)	50.0 – 92.1	68.3	7.68
Pregnancy duration (weeks)	28 – 36	31.6	2.13
Number of pregnancies	1 – 6	1.7	1.07
Number of children	1 – 6	1.6	1.04

N = 202

Table 3 shows the scores for neuropsychological test (NCTB) that was carried out on the respondents. It took about 30–45 minutes to complete all the 7 types of NCTB test. Standard Score Index Values were calculated from the raw scores and used for all statistical analysis.

Figure 2 shows the standardized NCTB score test distributions, which were normal ($p > 0.05$).

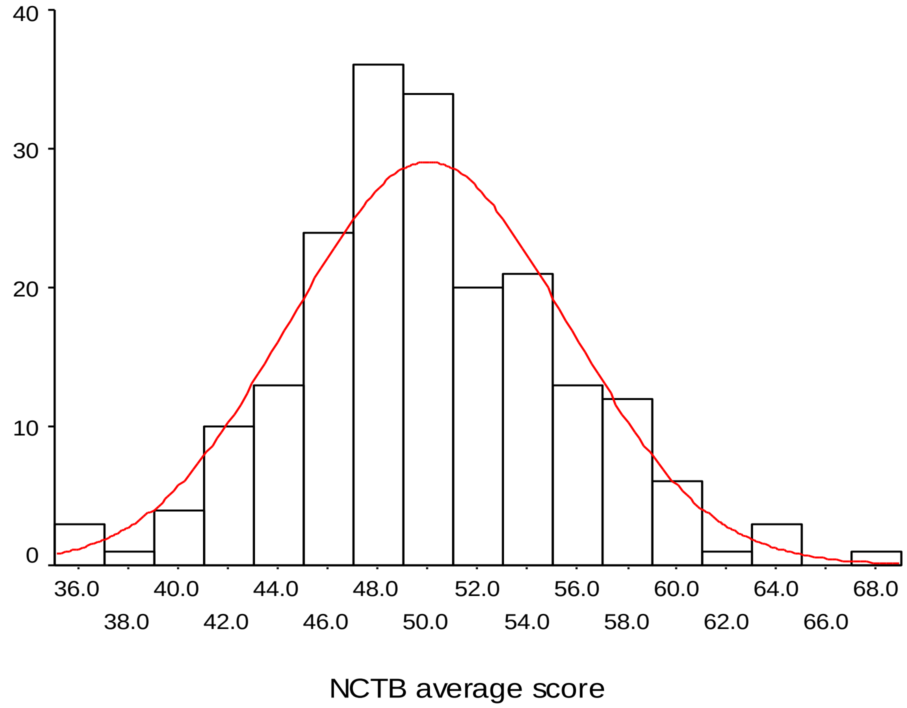

Fig 2. Distributions of Neuropsychological Scores

Table 3. Neuropsychological Scores (NCTB) of Pregnant Mothers

Neuropsychological scores (NCTB)	Range	Mean	Std. Dev.
Digit Symbol	29.0 – 78.3	50.0	10.00
Pursuit Aiming	24.5 – 80.0	50.0	10.00
Trail Making	26.4 – 73.1	50.0	10.00
Digit Span	35.8 – 85.2	50.0	10.00
Benton Visual Retention Test	24.8 – 67.3	50.0	10.00
Santa Ana Manual Dexterity	23.1 – 70.8	50.0	10.00
Reaction Time	23.5 – 72.0	50.0	10.00
Total Score Total Score	36.3 – 67.6	50.0	5.54

N = 202

Table 4 shows the correlation between blood lead and each NCTB test. The total NCTB scores also showed inversely significant correlation with the respondents' blood lead except for the Pursuit Aiming and Santa Ana Manual Dexterity tests. The linear model shows that about 21.3% of the variations in blood lead contributed to the neuropsychological scores. Table 5 shows that the total NCTB scores were influenced by the respondents' blood lead, age, weight and height after all the confounding factors were adjusted. This model shows that these factors contribute 27% of the variations in the NCTB scores.

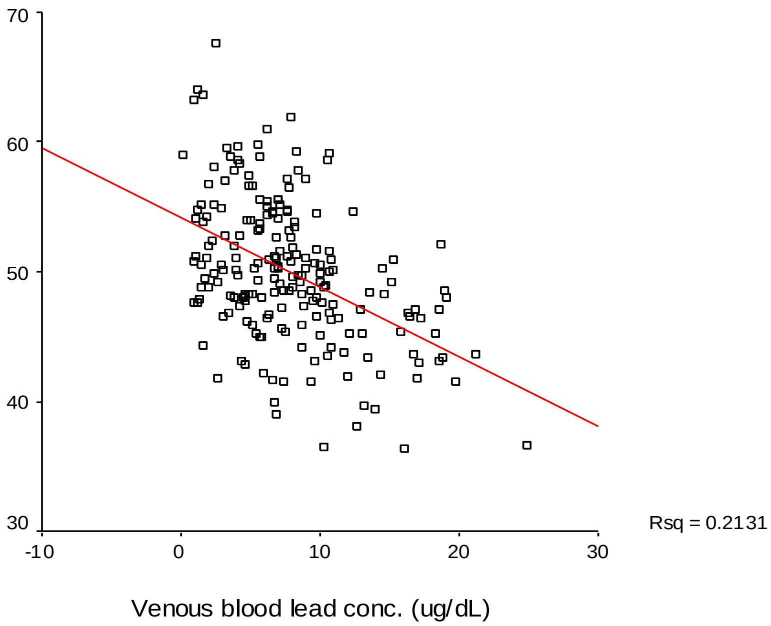

Fig 3. Correlation Between Blood Lead Concentrations and Neuropsychological Scores

Table 4. Correlation Blood Lead and Neuropsychological Scores

Neuropsychological test (NCTB)	**Blood lead (µg /dL)**	
	r	**p value**
Digit Symbol	–0.347	< 0.001**
Pursuit Aiming	– 0.021	0.762
Trail Making	– 0.254	< 0.001**
Digit Span	– 0.447	< 0.001**
Benton Visual Retention Test	– 0.256	< 0.001**
Santa Ana Manual Dexterity	– 0.016	0.817
Reaction Time	– 0.450	< 0.001**
Total score	–0.462	< 0.001**

N = 202

** Significant at $p < 0.01$

Table 5. Correlations of Blood Lead on The Neuropsychological Scores After Adjustment of Confounders

Dependant variable (Mean Neuropsychological score)	**Regression coefficient β**	**Statistict**	***p value***
(Constant) c	61.74	7.42	< 0.001**
Blood lead (µg /dL)	– 0.47	– 7.51	< 0.001**
Age (years)	– 0.15	– 2.40	0.017*
Weight (kg)	0.12	2.67	0.008**
Height (m)	– 0.10	– 1.61	0.110
Educational level (years)	0.08	1.18	0.239
Household income (RM)	– 0.13	– 1.79	0.075

N = 202

** *Significant at $p \leq 0.01$* F value = 12.787, $p < 0.001$

* *Significant at $p \leq 0.05$* $r = 0.531$, $R^2 = 0.282$

DISCUSSION

The mean blood lead of the respondents was 7.78 µg/dL (Figure 2), which is more than the blood lead of electronic industries soldering workers (6.10 µg/L) (4). Pregnant women need an optimum nutrient such as Ca^{2+} and Fe^{2+} or Fe^{3+}, for the growth of the babies (5,6). The body tends to absorb lead if the calcium and iron intake were insufficient in the diet. Lead in the mothers' blood systems has a potential of being transferred to the fetus through the placenta and this process began 2–3 months at an early stage of pregnancies. Blood lead concentrations for pregnant mothers should not exceed 10 µg/dL (7). However, almost 27% of the respondents have blood lead concentrations of more than 10 µg/dL. Studies (8) in African reported that mean blood lead for pregnant mothers who live in the city and the rural ranged from 0.83 to 99 µg/dL. The difference of those data was significantly difference. This proves that environment can influence lead concentrations in the blood. There was no significant relationship between blood lead with age and the gestation period. However, the mean blood lead in previous study was higher than this study.

Another study (9), on pregnant women reported that the mean blood lead concentration was 8.59 ± 4.45 µg/dL and about 27.8% respondents had blood lead concentrations higher than 10 µg/dL. The study found that housewives had higher blood lead (9.55±5.5 µg/dL) than those working in offices (7.44±2.77 µg/dL), factories (8.61±3.39 µg/dL) and shops (7.01±3.13 µg/dL). However, the difference was not statistically significant. Study by (10) reported that the mean blood lead for women in the Avon are of the UK was range 0.41–19.14 µg/dL. Studies at Port Pirie, Australia (11) reported that 646 women who are 30 to 36 weeks pregnant had an almost similar mean blood lead level of 7.2 µg/dL and 28% had blood lead of more than 10 µg/dL.

In general, neuropsychological scores were calculated from the 7 tests in the NCTB. Correlation tests indicated that blood lead for these pregnant mothers had an inverse significant correlation with Digit Symbol, Digit Span, Trail Making, Benton Visual Retention Test and Reaction Time (Table 4).

Only Pursuit Aiming and Santa Ana Manual Dexterity scores were not significantly correlated with blood lead (Table 4). The NCTB test result shows that pregnant mother with high blood lead have difficulties in concentrating and have short–term hearing and visual abilities (Digit Span Test, Benton Visual Retention Test). They have slow motor speed through vision (Digit Symbol Test) slow reaction toward visual stimulation (Reaction Time Test) and low attention ability, visual scanning and visual motor trailing (Trail Making Test).

In Figure 3 Shown ultiple regression test result demonstrated that mean neuropsychological score for pregnant mothers were influenced by blood lead (β = –0.56, p < 0.001), age (β = 0.12, p < 0.017), weight (β = 0.12, p = 0.08) and height (β = –0.01, p = 0.050). The model was significant (F = 18.23, p < 0.001) with the R2 value, which shows that 27% of the variations in the NCTB scores were influenced by the variables shown below:

NCTB mean score = 65.71 – 0.56 (blood lead) – 0.15 (age) – 0.10 (height) + 0.12 (weight)

Previous studies showed that blood lead among female workers had the abilities to lower the NCTB score (12,13). Studies (12) showed that 140 female factory operators had a mean blood lead concentration of 30.77 µg/dL and it was inversely correlated only with the Reaction Time test (r = –0.201, p = 0.017). Meanwhile (4) found that mean blood lead for female soldering workers at an electronic factory was 6.1 µg/dL, and the comparative group was 4.6 µg/dL. The respondents' blood lead had significant relationships with Digit Span Test (p = 0.003), Santa Ana Manual Dexterity Test (p = 0.007) and total NCTB scores (p = 0.001). The exposed workers had significantly lower mean score compared to unexposed workers for Digit Symbol Test, Trail Making Test and Pursuit Aiming Test.

Pregnant mothers with high blood lead had problems with the ability to concentrate and have poor short–term auditory and visual memory and have the inability to organize geometry patterns in space and memorizing them. They have poor perceptual motor speed and fail to match between symbol and digits. They also had slow reaction to stimulation due to poor ability to pay attention and low attention ability, which cause poor visual motor tracking as well as poor visual scanning.

Blood lead concentrations, age, weight and height influenced 27% of the variations in neuropsychological score after adjusting for confounders. About 1 µg/dL increment in blood lead will reduce 0.4 of the neuropsychological mean score of these pregnant mothers.

CONCLUSIONS

In conclusion, even though the blood lead concentration is quite low, it affects the neuropsychological ability of the respondents. Digit Symbol, Digit Span, Trail Making, Benton Visual Retention and Reaction Time test scores had significant inverse correlations with the blood lead.

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CONFLICT OF INTEREST

There are no conflicts of interest.

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