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MALONDIALDEHIDE (MDA) URINE AS AN EARLY MARKER OF DEVELOPMENTAL DISORDERS OF CHILDREN LIVING AROUND GOLD MINES

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Abstract

Children born to mothers living around gold mines are at risk of mercury exposure (Hg) and can cause developmental disorders. These developmental disorders can be detected early through stress oxidation mechanisms based on Hg toxicity that directly harm brain cells. It can be detected early on from the level of DNA damage, which is malondialdehyde (MDA) in the urine. Examining children's MDA urine levels near gold mines is the aim of this study. The Observational Research Method performs measurement of MDA of baby urine with TBARS examination of 16 babies in the age range of 2-14 weeks babies who live around the gold mining village Kalirejo Prefecture Kokap district of Kulon Progo Yogyakarta. The result was a rate of 3.23 µmol/L of MDA in baby urine, which is above the normal level of 1.03 µMol/L. So it can be concluded that the high level of MDI in the baby's urine is an early indication of a child's developmental disorder living around the gold mining.

Keywords: ***Gold mines, child developmental disorders, Malondialdehid***

1. INTRODUCTION

Pregnant mothers living around gold mines are at risk of exposure to mercury (Hg) and giving birth to babies with developmental disorders. The most critical periods of fetal developmental disorders are pre-conception, pregnancy, and postnatal. This is because it is the stage of development and growth of the brain and other organs.(J. *et al*., 2002). Pregnant women who are exposed to Hg alkyl can cause damage to the fetal brain so that the baby is born with disability. A concentration of Hg 20 µg/L in the blood of a pregnant woman causes damage to the fetal brain. (Palar, 1994 dalam Widowati,2008). This transplacent exposure is the most dangerous because the fetal brain is very sensitive (WHO 2007). The main organ affected by mercury poisoning is the neurological system, especially organic metal compounds. Metal Hg is fat-soluble, easily passing via the blood-brain barrier and entering the brain system. (Cope.WG.*et.al*, 2004; Risher. JF *et.al* 2007). This developmental disorder's mechanism in the baby occurs when there is continuous exposure to Hg in the mother before and during pregnancy as well as after the baby is born. One heavy metal is hg, which can induce oxidative stress that is potentially harmful to health (Crespo-L *et al*., 2009;Houston, 2011). Oxidative stress from Hg interactions causes neurotoxicity (Gasso *et al*.,2001; Belletti *et al*., 2002; Huang *et a*l., 2008; Farina *et al*., 2011). Hg will interact with macromolecules since it is a reactive species like lipid,protein, and DNA. The result of This substance interaction produces DNA aduct, a component of genotoxicity. A member of the DNA aducts is Malondialdehide (MDA) that able to detect damage to DNA. MDA can be eliminated by urine. MDA has been extensively employed as an oxidative stress biomarker and carcinogenesis (Huang *et al*., 2008). The assessment of oxidational stress by observing its biomacteria is an indicator in evaluating exposure to chemicals, as it can provide preliminary information about the pathogenesis of a disease before the onset of health effects. (Ziech *et al*.,

2010). MDA causes an imbalance of amino acids and glutamate as well as triggers neuro apoptotic pathways (Restuningwiyani *et al*., 2018), and excessive nerve apoptosis can lead to long-term brain dysfunction. (Shoji *et al*., 2014).

2. RESEARCH iMETHOD

An Obsevasional Study to Know Malondialdehide (MDA) as an Early Marker of Child Developmental Disorders. A total of 16 babies born are assigned as respondents. The minimum number of children born to a mother who has been staying for 3 years at maximum during her lifetime in the area surrounding the Golden Village of Kalirejo, Kokap district of Kulon Progo, Yogyakarta. Ethical clearance for conducting this research was acquired from the Committee on Medical Health Research Ethics, University of Gadjah Mada's Medical Faculty (Ref: KE / FK / 1036 / EC / 2017). Declaration of readiness to sign this informed consent form in order to become a Respondent. The signature is made after obtaining an explanation of the research, understanding the purpose, method or implementation of research and the risks that arise during the research.

Baby urine samples are collected in the morning after waking up, before eating or swallowing any ice fluid. Baby urines are taken in the baby's age range of 2 - 14 weeks (stage I), and 14 - 26 weeks. (Tahap II). Urine is taken using a urine pot, and the identity of the subject (name and stage of collection) is written on the label paper that has already been placed and stored in a refrigerator or thermos, then stored at a temperature of -80 0C until TBARS examination. The urine MDA examination is started by making TBARs cheapest using TBA Reagen-TBA Buffer: 40.5 milliliters of 3.5 pH 20% acetate acid, with a concentration of 1 N NaoH, 13.2 ml of 82% Sodium Dioxide Sulphate (SDS chemical material), 40,5 ml of 0.8% TBA, then added aquadest to a volume of 100 ml. Extrusion solution of butanol is dispersed and made with butanole combination: Bidest: pyridine = 15 : 3 : 1. The standard TMP (TetrameThoxypropane) used is 2 µL/mol, 4 µL /mol, 6 µl / mol, 8 µl/mol and 10 µ L / mol. The examination was conducted by taking 1 ml of sample plus 4.0 ml of TBA in incubation at 90 oC for 80 minutes. (1 jam 20 menit). Then cool in ice, then add 4.0 butanol extract and centrifuge at 3000 g. Then read it at the 510,532 and 560 nm waves using Elisa

3. RESULTS AND DISCUSSION

As ifor ithe iresults iof ithe istudy, iwe ican iread iin iTable i1 iand iTable i2:

Table 1 below shows that the rate of MDA in baby urine is 3.23 µmol/l Median±SD is 2.31±2.35 µmol / l, with the lowest and highest MDA levels of 0.83 - 8.96 and 0.69 - 10.24 µmol./ l.

Tabel 1 Table 1 Descriptive Data Analysis MDA Rate of Baby Urine

Variable	Mean	Median	SD	Minimum-Maksimum	95% CI
MDA Baby (µ Mol/L)	3,23	2,31	2,35	0,83 - 8,96	1,98 - 4,48

The following table 2 shows the results of a survey of 16 infants, of whom 13 infants (81.2%) at the age of 2-4 weeks had MDA levels above normal human levels (1.03 µMol/L) and 3 infants were below normal humans

Table 2 Frequency Distribution of Baby Urine MDA Rates

No.	MDA Rate	Age 2-4 weeks	
		n	%
1.	< 1,03 µMol/L	3	18,8
2.	>1,03 µMol/L	13	81,2
	Jumlah	16	100

One of the factors that causes oxidative stress is MDA. MDA is the primary byproduct of polyunsaturated fatty acid oxidation in body fluids or tissues and is an indicator of lipid peroxide (Del Rio *et al*., 2005). (La Maestra *et al*., 2011; Rahardjani, 2016). MDA interacts with a variety of biological macromolecules, including proteins, nucleic acids and alters their functions and then interferes with neural development. (Li *et al*., 2010). So it could be said that 81.2% of babies born in the village of Kalirejo district Kokap are at risk of developing developmental disorders. MDA plays a role in nerve damage that causes seizures and subsequent nerve dysfunction. MDA can bind and react to proteins and nucleic acids that play a part in the development of nerves. Many studies have shown that MDA causes an imbalance of amino acids and glutamate as well as triggering neuro apoptotic pathways. (Restuningwiyani *et al*., 2018). Shoji et al., 2014 stated that oxidative stress can trigger apoptosis in the brain, and excessive nerve apoptosis can lead to long-term brain dysfunction.

Numerous investigations on animals have noted that oxidative stress underpins the brain effects of fetal exposure to Hg. (Stringari *et al.*, 2008; Huang et al., 2011; Zhao *et al*.,2014). But still, research (Al-saleh *et al*., 2016) demonstrated a possible mechanism of Hg in organic form with oxidative stress that contributes to delayed baby nerve development.

Increased production of ROS induces cellular and molecular changes that cause hyperexcitability or death of neurons. (Rodriguez *et.al*., 2013 dalam Perrone, n.d.). Neurons in the brain are very sensitive to oxidative damage because the membranes of neurons are mostly formed by phospholipids. (Waldbaum *et al*., 2010). So oxidative damage may be important Within the etiology of various neurodegenerative diseases (Gandhi & Abramov, 2012). Infant MDA is related to developmental aspects, also found in the Restuningwiyani et al., 2018 study of infant MDA levels and their relationship to development in infants suffering from seizures Status Epilepticus using the Bayley III scale, which states that generally the MDA level is adversely connected with the results of the Bayleys scale III test. MDA has a negative correlation with cognitive composites ($r = -0.8000$, $p = 0.000$), language composite ($r = -0.648$, $p = 0.000$), and motoric composites. MDA can bind and react to proteins and nucleic acids that play a role in nerve development. Many studies have stated that MDA causes an imbalance of amino acids and glutamate and triggers neuroapoptotic pathways. (Restuningwiyani *et al*., 2018). For that, Hg exposure to mothers and babies must be stopped immediately so that oxidative stress continues.

4. CONCLUSION

High levels of MDA in babies born and living around the gold mining village of Kalirejo, Kokap district of Kulon, where 80% have urine MDA levels above the normal level of a person (1,03 µMol/L). This indicates that 80% of babies will experience developmental disorders if not addressed immediately

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