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The impact exposure metal fume and vapor with total IgE and total IgG

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Abstract: Blacksmith centers which produce agricultural tools, household appliances, carpentry tools, souvenirs, propeller and other vessels are located in the District Hulu Sungai Selatan, South Kalimantan Province. The Blacksmiths during their works did not use personal protective equipment, they were always exposed to metal fume and vapor, and compounds resulting from the combustion process in a high temperature (>600^{o}C) with results ab normalization in the total IgE and total IgG levels. The objective of the investigation was to assess the impact between exposure of metal fume and vapor with the total IgE and total IgG levels. The study was analytic observational, and cross sectional design conducted in the Districts of Hulu Sungai Selatan, South Kalimantan Province Blood sampling, measuring of metal fume and vapor, were conducted at Kandangan hospital, and Balai Hiperkes and keselamatan Kerja South Kalimantan Province, respectively. Whereas determination of total IgE and total IgG levels was carried out at Prodia laboratory Jakarta - Indonesia. The population of studies was the entire blacksmiths in districts of Hulu Sungai Selatan, South Kalimantan Province, Indonesia. The sampling procedure was based on purposive sampling predefined by inclusion and exclusion criteria with a sample of 38 units and 38 blacksmiths with two population proportion hypothesis. Result were analysed observational, and cross sectional design using logistic regression, and test of Partial Least Square (PLS). Result were logistic regression a significant correlation due to exposure of metal fume, and vapor with the ab normalization total IgE by p:< 0.05; and the Partial Least Square (PLS) indicated the presence of a significant correlation of metal fume, and vapor with the ab normalization of total IgG with R^2: 0.1569. In conclusion, this study demonstrates the presence of a positive and significant impact and correlation due to exposure of metal fume and vapors with of total IgE and total IgG levels.

Key words: *Impact; Metal fume and vapor exposure; Total IgE and total IgG serum levels*

1. Introduction

The Blacksmith centers located in the district of Hulu Sungai Selatan, South Kalimantan Province, Indonesia is a center for the production of the people that have been done from generation to generation until now in the manufacture of agricultural equipment, household appliances, carpentry tools, souvenirs, propeller and others of metallic substrates/metal (Husaini, 2011). The result of the combustion process and smelting metal with temperature > 600oC (Fauzi, 2000) can enter into the body's immune system and can lead to an increase in allergic inflammation. Through this mechanism, particulate / air pollutants can be an important contribution to the increase in the prevalence and morbidity of allergic rhinitis and other respiratory diseases. The role of particles (dust), gas, metal fume and DEP (Diesel Exhauster Particle) and their compounds can enhance the immune response to IgE production (Prasad, 1987; Bastain, 2003). Then also can inflammation and infection of the respiratory tract and lungs cause, thus increasing the entry into the body of allergens and antigenic Blacksmith (Andre et al., 1998). The Blacksmith besides getting exposure to various pollutants such as metal fume, various vapor especially iron vapor and any Diesel Exhauster Particles (DEP) and the compound but is also influenced by the lack of the presence and use of Personal Protective Equipment (PPE) as well as the availability and implementation of Standard Operating Procedures (SOP).

Air pollution containing particulates such as metal fume and vapor including other particles such as Diesel Exhaust Particles (DEP) and its compounds, able to potentiate chronic inflammatory processes as well as the response to the acute symptoms of the respiratory tract and causes induction of apoptosis through generation of Reactive Oxygen Radical (ROR) that causing loss of surface membranasimetri and DNA damage, dermatitis or other skin allergies due to exposure to metal fume and can trigger the/ trigger chronic mild though, the inflammation in the lungs and showed improvement tumuorigenesis, the production of IgE can affect (Knox et al., 1997; Muranaka et al., 1986; Suzuki and Kanoh, 1993). Specifically found cell hyperplasia after intratracheal

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or inhalation response shows the effect that helps in the production of IgE (Sagai dkk, 1996; Miyabara et al., 1998; Ichinose et al., 1997; Kobayashi and Ito, 1995; Kobayashi et al., 1997; Tenkate, 1999; Erhabor et al., 2001; Miyabara et al., 1998; Heo et al., 2001). In the work every day, do not use a Blacksmith Personal Protective Equipment (PPE) that is always exposed to various pollutants such as vapor, gas and metal fume and if this continues for a long time to decrease the immune system and there is a variety of occupational accidents (Husaini, 2010). Pollutants from activities such as metal fume of the Blacksmith and vapor and other particles such as DEP and its compounds when exposed Blacksmith can increase the permeability of the mucosa of the respiratory tract thus increasing revenue antigens and allergens, as a result of repeated exposure to organic antigens or chemicals present in the work environment (Husaini, 2014). Repeated inhalation of antigens that stimulate an immune response in the form of inflammation in the interstitial tissue, alveoli and terminal bronchioles and one of the diseases that often occur in people who are associated with hypersensitivity pneumonitis job is classified in the group of respiratory diseases and other infections(Boedina, 2010; Epler, 2000; Setiono, 2000).

The basis of this disease is the interaction between the external antigens and the host immune system (Selman, 1998). To vulnerable groups, such interactions lead to type III hypersensitivity reactions (immune complex hypersensitivity) and IV (delayed or cellular hypersensitivity). Factors that determine a person vulnerable to hypersensitivity pneumonitis after antigen sensitized so far not clearly known. Some studies have found that genetic factors associated with a person's vulnerability to the disease. Obtained an increase in the human leukocyte antigen (HLA) B8 (the Caucasian), HLA DQ w3 (the Japanese), HLA DR7 (the Mexico), HLA DRB1 and HLA DRQ1 in patients with hypersensitivity pneumonitis (Selman, 1998; Schuyler, 2001). The gene that encodes HLA gene is closely related to the immune response of the major histocompability class II complex (MHC class II). The interaction of antigen, the T- lymphocytes and antigen presenting cells (APC) requires MHC II. Different MHC affinity to the antigen affect vulnerable or not to hypersensitivity pneumonitis. Factors that play a role is the polymorphism of tumor necrosis factor alpha (TNF α) associated with the inflammatory response and receptor fragment crystallisable (Fc) associated with the formation of antibodies (Buerke et al., 2001). Exposure to the antigen must be repeated until the immune system has been sensitized. Inhaled antigen will be captured by alveolar macrophages and presented by APC to CD8 T- lymphocytes that have been sensitized by MHC class II. CD8 + T-lymphocytes are sensitized to activate plasma cells to produce IgG antibodies form antigen-antibody immune complex (precipitins). The immune complexes activate the alternative complement pathway and alveolar macrophages.

The pollutants various such as particles of metal fume, iron vapor and any DEP elements especially to get into the lungs of PAH (Polycyclic Aromatic Hydrocarbon) Blacksmith, then trigger allergic reactions and cause a variety of infections, and in the lungs of particles originating from the DEP has toxic effects that exacerbate respiratory disease has been before, especially bronchitis, COPD, cystic reaction and of highly reactive, toxic and potentially fibrogenik (Prasad and Bondy, 1987; Kelleher et al., 2000) and is capable of causing inflammation and increased permeability of the mucosa and increased endotoxin which is sources of bacteria (Bonner et al., 2007; DiazSanchez, 2000a; Becker, 1996;Terada et al., 1996). Metal fume received by workers in a long time and continuously cause can cell changes and cause the genotoxic and this is consistent with the research of Costa (Costa et al., 1993) that the workers are always exposed to the metal fume has a cross-links protein DNA content as a result of excessive exposure to cross-linking between genes and have potential as a genotoxic effect.

By reason of the aforesaid background researcher / writer interested in studying the effect of exposure to metal fume and vapor with of total IgE and total IgG serum levels of Blacksmith in Distric of Hulu Sungai Selatan, South Kalimantan, Indonesia. This study uses observational analytic cross sectional study (Husaini, 2010).

2. Material and method

The studies were conducted over the period of 20 months from February - November of 2011 - 2013. The study was conducted at the unit of blacksmiths, namely in district of Hulu Sungai Selatan, South Kalimantan Province, Indonesia. Blood sampling was dose to measure of metal fume and vapour, were conducted at Kandangan hospital, and Balai Hiperkes and keselamatan Kerja South Kalimantan Province, respectively. Whereas determination of total IgE and total IgG levels was carried out at Prodia laboratory Jakarta - Indonesia. The inclusion criteria of the subjects were as follow age 25 - 50 years, working period of at least 5 years, had never worked on a similar job before, never smoking. While the exclusion criteria were those who refused to participate in the study, had an allergy, pulmonary tuberculosis and other lung infections. Techniques of sampling in this study was purposive sampling that meet the inclusion and exclusion criteria were 38 units, and 38 blacksmiths. The independent variables were metal fume, and vapor, while the dependent variables were total IgE and total IgG serum and the controlled variables were age and year duration of work. Chemicals and equipment used in this study were water bath, spectrophotometry brand Biosystem BTS-305 type, brand hetto oven, pH meter (cyberscan), vortex mixer VM-300, fridge (sharp), glassware (pyrex), gas analyser (Factory by; USA, Tech).

3. Result and discussion

Table 1: Conditions of total IgE levels, total IgG and Mixed Serum of Blacksmith

Variable	N	Immunoglobulin					
		Normal	%	Abnormal	%	Mixed	%
Total IgE	38	14	37	24	63	13	34
Total IgG	38	15	39	23	61		

Notice: This study the value of alpha (α) is 0:05.
N = Number of Samples Overall.
% =Percentage of Total Respondents

The results of the study to assess the correlation of metal fume and vapor exposure and with an increase of total IgE levels normal Blacksmith done with logistic regression analysis found a significant correlation (p: 0.032 <α, and α values in this study 0.05) and the value of R^2: 35.6 %. Then to the results of other studies found a significant correlation with the increase of the normal range in total IgG levels using the test Partial Least Square (PLS) with R^2: 0.1569 or 15.69% which means that the overall contribution of pollutants to the enhancement of the normal range in total IgG levels by of Blacksmith 15.69% were interpreted in test conditions PLS strong enough or harmful effects on the immune response in this case the total IgG levels (Husaini, 2014). The assessment of air quality in metal fume in the Blacksmith location = 4479 mg / Nm^3 and vapor = 5925 mg / Nm^3 * (notice * above the threshold by the Indonesian Government = SE RI-Number: 01 / Men / 1997 with ≤ 5 mg / $Nm^{3)}$ (Government of Indonesia-SE Menaker RI Number 01/Men/1997).

This study, which examined immunoglobulin is kind of total IgE and total IgG with the intent to see the cause or pollutants common in Blacksmith unit ie metal fume and vapor as well as the DEP and its compounds are also other considerations that a Blacksmith in addition to producing pollutants the climate also or hot working temperature, the presence of noise and vibration that greatly affects the speed of chemical reactions in the air especially in the body where the Blacksmith whenever work is always exposed. Therefore, it is very difficult to specifications contributing to the increase of the normal range of specific IgE and IgG in Blacksmith and in this case is a limitation in this study are expected in future studies can be to examine IgE and IgG specific to the cause as well (Husaini, 2014).

The results of these studies showed significant above the normal limit the increase of total IgE and total IgG levels as a result of pollutants various of Blacksmith such as metal fume and vapor and DEP (Diesel Exhaust Particle) and their compounds, in this case probably due to the nature or characteristics of substances or molecules are released into the air react with each other that are synergistic or additive nature or the accumulation of substances or molecules either in the air or in the body, so that although the levels of substances or molecules are released in the air is still below the Threshold Limit Values (TLV) in this case Number-SE. 01 / Men / 1997 (Government of Indonesia-SE Menaker RI Number 01/Men/1997) is possible can increase total IgE levels and at the same time also increases the total IgG levels in the body of Blacksmith (Husaini, 2014).

Other Factors affect the likelihood of an increase in the normal limit of total IgE and total IgG levels where of Blacksmith worked without regard to principles of Occupational Health and Safety (OHS) is mainly self-protection such as masks, muzzles, headgear and leather so if continuous exposure of Blacksmith will facilitate the entry of antigens and allergens into the body which then stimulate can an immune response that can increase the permeability of blood artery and increase airway resistance and can increase total IgE antibody antigen response and total IgG (Husaini, 2014). This is partly consistent with the research of Diaz-Sanchez (Diaz-Sanchez, 2000a) that DEP has important components of PAH resulting from the combustion of raw material metal or still attached to the oil and used oil will have risk factors for elevated of IgE and IgG levels.

The pollutants various such as particles of vapor and DEP elements mainly PAHs to get into of Blacksmith lungs, then trigger allergic reactions and cause a variety of infections, and in the lungs of originating particles from the DEP has toxic effects that aggravate existing respiratory diseases previously, especially bronchitis, COPD, cystic reaction and of highly reactive, toxic and fibrogenik potentially and is capable of causing inflammation and increased permeability of the mucosa and increased endotoxin which is a source of bacteria (Bonner et al., 2007; Diaz-Sanchez, 2000a; Becker, 1996; Terada et al., 1996). Furthermore opinion of Bonner (Bonner et al., 2007) explains that the DEP particle and its compounds, especially vanadium and zinc types predisposing or stimulate cells lung to release inflammatory mediators to cellular signaling pathways activate leading to an increase or decrease in gene expression and this causes the cells that birth reactivity give of ROS, which ROS this is able to the receptor tyrosine kinase activated, EGFR and transcription factors such as NF-kB, STAT-1 and MAP kinase. The next process of ROS inhibit PTP can (protein tyrosine phosphatase) were associated with an important part of the intracellular EGFR, as a result of inactivation of PTP causes phosphorylation

of EGFR occurs and as the end of the MAP kinase pathway of the activation.

In the context of particles inhaled possibility that the inability to clean up toxic particles from the lungs through phagocytosis as well as continuous or repeated exposure can move an excessive inflammatory response that leads to irregular tissue remodelling and fibrosis. Initiation of this pathway may occur due to the interaction with macrophages alveolar, epithelial cells or direct interaction with interstitial fibroblasts (Williams, 1986). Transition metal seems to be the main mechanism of oxidative stress and inflammation. Cases due to exposure to welding aluminum particles were able to induce pneumoconiosis and find areas of severe fibrosis and are also surrounded by macrophages containing particles (Hull and Abraham, 2002).

The metal fume received by workers in a long time and continuously cause can cell changes and the genotoxic and this is consistent with the studies Costa (Costa et al., 1993) that the workers are exposed always to the metal fume has a cross-links protein DNA content as a result of excessive exposure to cross-linking between the agent and have potential as a genotoxic effect. Metals such as manganese and copper particles that enter the body are stored in the nasal mucosa and transported to the brain that would be neurotoxicity (Erikson et al., 2004).

Air pollution containing particulates such as metal fume and vapor including other particles such as Diesel Exhaust Particles (DEP) and its compounds, able to chronic inflammatory potentiate processes as well as the response to the acute symptoms of the respiratory tract and causes induction of apoptosis through generation of Reactive Oxygen Radical (ROR) that causing loss of surface membrane asymmetry and DNA damage, dermatitis or other skin allergies due to exposure to metal fume and trigger can chronic mild though, the inflammation in the lungs and showed improvement tumuorigenesis, can affect the production of IgE (Knox et al,1997;Muranaka,1986,Suzuki,1993).

The other thing reasonably suspected to take effect in the increase of the normal total IgE and total IgG levels of Blacksmith are some of the metal materials used by Blacksmith are car spring and many metal plate attached to oil and used oil (there is derived from the source, and there are intentional given oil and waste oil to avoid rust) when burned at high temperatures (> 600^{o}C) resulted in unravelling some of the metal particles and when it enters into the body damage can of the body cells, various diseases causing of the respiratory tract and lungs (Husaini,2014). This is consistent with the studies from (Kennedy et al,1999;Dye et al,1999;Diaz-Sanchez et al,2000b;Louis,1998) that if the metals are heated, the oil will break down into several compounds such as vanadium and copper, Polycyclic Aromatic Hydrocarbon (PAH), as well as a bacterial endotoxins source are linked to each other and influence each other towards the body target and able to mediate cell cytokine gene expression induced by residual oil and ash that pollute the environment when working of Blacksmith, bad for their health. DEP chemicals also induced activation of stress protein kinase activated that plays a role in cell apoptosis pathway.

Other factors, the possibility of environmental pollutants such as working of Blacksmith metal fume and vapor and the DEP and its compounds there are no individual allergens or Blacksmith sensitive to pollutants which to exposure (Husaini, 2014). This is in studies Knox (Knox et al., 1997) which states that exposure after to allergens, especially in individuals who are hypersensitive to certain particles such as DEP and its compounds albeit at a low dose rate will act as adjuvants to allergens that enter the respiratory mucosa. The studies Kobayashi (Kobayashi and Ito, 1995) as a result of particles decompose at high temperatures, such as DEP and other metal particles when to enter the body increase can the permeability of blood artery and parallel with the resistance is increased in the airways and simultaneously IgE levels.

The foregoing is also consistent with the studies Diaz-Sanchez (Diaz-Sanchez et al., 1997a); Lee (Lee, 1998) that when the vapor or particles including elements of the DEP and its compounds are human or Blacksmith exposure in a long time and continuously when into get the body, it increase can the production of Th2, including IL-13 in individuals exposed . This study shows that the metal particles and the DEP increase can the incidence of allergies, at least in part have increased production of Th2. It is entirely possible that the interaction of epithelial fibroblasts is important in the pathogenesis of fibrosis respiratory see. Air pollution containing metal particles and DEP also activates the epithelial to produce inflammatory mediators in turn mesenchemal underlying. This studies Burnet (Burnet, 1986) that exposure to the antigen must be repeated until the immune system has been sensitized. Other factors that take effect on lung function decline in this case the restrictive disorder, obstructive and combined (mixed) as well as the increase of normal total IgE and total IgG levels in Blacksmith are the reactions various of chemical substances in the work environment such as air pollutants metal fume and vapor as well as the DEP elements and their compounds at levels of exposure that is long and constantly will affect the components or parts nostrils, bronchi, lungs and the body's immune response (Husaini,2014). This is in line with the results of studies related to vapor and particles from studies (Miyabara et al., 1998; Ichinose et al., 1997; Yanagisawa, 2006; Ohta et al., 1999; Hatch et al., 1985) on lung susceptibility to bacterial infections and cytotoxic effects on macrophages. In addition, genetic susceptibility associated with increased risk of respiratory diseases and other infections due to exposure to metal fumes and particles. Allergic reactions and inflammation in the airways hyper reactivity of animal models have shown that the increased production of allergy antibodies and generation of

Th2 responses generated by the interaction between allergens and pollutants can also lead to allergic effects in the respiratory tract caused by work.

The results of measuring pollutants in the work environment in this study, although not describe the actual levels of these pollutants in the body of the Blacksmith due to limitations in research that does not measure levels of substances or molecules in the blood sample, therefore it is advisable to do further research for measurement and analysis with other compounds or the reaction products with other compounds in the work environment or in the body of the Blacksmith remember that the compounds or molecules are released into the working environment very easily bind or reaction with each other and will also create the possibility of secondary pollutants or substances other secondary more toxic, reactive and synergy despite measurable levels of pollutants in the air free work environment is still below the Threshold Limit Value (TLV) which has been determined that (Husaini, 2014). To anticipate the distractions various in the workplace result of pollutants various should be cautious in giving a conclusion results from measurements of air quality in the work environment, especially when the results of measurement of pollutants various or substances still below the Threshold Limit Value (TLV) imposed a State, including Government the Republic of Indonesia in this Regulation valid is the Number: SE. 01 / Men / 1997 (Government of Indonesia-SE Menaker RI, Number 01/Men/1997), because the slightest substance or molecule is released into the work environment does not guarantee the working environment including the workers to be safe, mainly related to the immune status of a person or relating to the nature or pollutants or substances of characteristics (Husaini, 2014).

A normalization or above the Threshold Limit Value (TLV) immune response (total IgE and total IgG) serum Blacksmith with a pollutants of variety, both are free and are the combined result of chemical various reactions in the air. When measuring and analysing pollutants various in the workplace has always been associated with the Threshold Limit Value (TLV) both in the air and pollutant levels in the body are then linked to the occurrence of immune response. Then also when analysed further that the contained pollutants in the working environment is easy to react or bind to substances or other molecules and is certainly relate also to the environmental conditions in which these pollutants are such a hot temperature, humidity, presence of noise and vibration as well as associated also with the nature or characteristics of each pollutant itself that is synergistic, additive, independent, and accumulative antagonist both in the workplace and in the body, therefore, that in order to measure air pollutants is not enough if only judged by the Threshold Limit Value (TLV) is based on the form of the pollutant itself, but also to be assessed on the basis of various chemical bonds and this is what distinguishes the research that already exists. Given that if two or more substances released into the air at the same time it will create a variety of chemical reactions in the air and also very difficult to predict against defects or damage to the human body when exposed to pollutants various although these substances are far below the Threshold Limit Value (TLV) determined by the Government of a State, including the Government of Indonesia (Husaini, 2014). The results of another study that distinguishes the work of others is that Blacksmith age group most common ab normalization or total IgG levels above the Threshold Limit Value (TLV) is in the age group above 38 years, while for ab normalization or total IgE levels above the value (TWA) is the age group above 35 years (Husaini, 2014).

Scientific contributions achieved in this study is that the pollutants are released into the air at the same time after the measurement of the pollutant levels one by one, although still far below the Threshold Limit Value (TLV) then do not warrant the creation of a safe working environment and including workers , so that the treatment of air pollutants and the cleanliness of the workplace in accordance with Standard Operating Procedures (SOP), control of resources and hazards potential in the workplace, including education, training and supervision by stakeholders by promoting the principles of Occupational Health and Safety (OHS) is necessary absolutely (Husaini, 2014).

3. Conclusion

In conclusion, This study demonstrates the presence of a positive and significant impact and correlation due to exposure of metal fume and vapor with of total IgE and total IgG levels of Blacksmith.

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