SERUM FERRITIN IN RELATION TO BIOLOGICAL PARAMETERS OF GASOLINE WORKERS

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ABSTRACT: The objective of this study was to evaluate the relation of serum ferritin levels to biological parameters in gasoline workers of Pathumwan area, by interviewing and collecting blood samples during their 6-8 hours workshift, from April to June, 2009. The purpose was to determine serum ferritin levels, hematological tests, kidney and liver function tests and enzyme cholinesterase. The results found that serum ferritin was significantly and directly related to serum glutamic oxaloacetic transaminase (SGOT, *Linear regression analysis, $p<0.001$*), serum glutamic pyruvic transaminase (SGPT, $p<0.05$) and inversely related to hemoglobin level (Hgb, $p<0.05$). These findings indicate that elevated ferritin levels in gasoline workers may serve as an important clinical marker for chronic liver disease in connection with decreasing hemoglobin level.

Keywords: Serum ferritin, Biological parameter, Gasoline worker

INTRODUCTION

Ferritin, a major iron storage protein, is the primary critical iron storage essential to iron homeostasis. In clinical medicine, ferritin is utilized as a serum marker of iron stores in the body which plays a critical role of both, diagnosis and management of iron deficiency and overload [1], causing pathologic consequences. Ferritin plays a role in a multitude of human diseases such as sideroblastic anemias [2], neurodegenerative disorders [3, 4], malignant disease [5] and inflammatory disorders such as hemophagocytic syndrome [6]. Serum ferritin remains a clinically useful tool for physiological and pathological processes. Gasoline worker is a high risk group exposed to volatile organic compounds (VOCs) such as benzene, toluene, ethylbenzene and xylene (BTEX), creating effects in hematological, neurological, immunological systems [7-11]. The preliminary study of gasoline workers in Pathumwan area found that 45.5% of 44 gasoline workers had lower hemoglobin level than normal, but higher levels of SGOT, SGPT and ALP at 9.1%, 15.9% and 38.6% respectively [12]. In addition, there was a significantly lower level of serum cholinesterase than in control groups *($p<0.05$)* [13], a risk factor for liver disease [14]. Thus, this study should be followed up to understand the cause of lower hemoglobin levels and their relations.

MATHERIALS AND METHODS

Study Population

83 men and 42 women from 11 gasoline stations in Pathumwan area were interviewed on their characteristics. Only 80 men and 26 women consented to collect blood samples during April and June 2009. Ethical approval was obtained from the Ethical Review Committee for Research Involving Human Research Subjects of College of Public Health Sciences (COA No 115/2008), Chulalongkorn University and written consent was obtained from all workers.

Blood sample assays

Hematological tests were determined by blood cell analyzer (Sysmex SF 3000), kidney function tests (serum BUN and creatinine) and liver function tests (serum SGOT, SGPT, ALP) by blood chemistry analyzer (Vitalab Flexor XL). Serum ferritin and total cholinesterase were analysed by a standard laboratory (Professional Laboratory Management Corp Co.,Ltd., Bangkok, Thailand).

Statistical analysis

The descriptive and linear regression analyses were performed for characteristics and relationship between serum ferritin and biological variables with SPSS for Window 17.0. The idea behind finding the best fit line is based on the assumption that the data are actually scattered in or around a straight line. If the scatter plot indicates that there is a linear relationship between the biological variables, then it is reasonable to use an expedient fit line to make predictions for y given x within the domain of x-values in the sample data. Reasons to use a Regression Model described the association between outcome and factors of interest, adjusted for confounders, determined important risk factors affecting the outcome and predicted the quantification of new cases [15].

RESULTS

The characteristics of 125 gasoline workers are shown in Table 1. The median serum ferritin of 80 male and 26 women workers were 213.1 and 84.8. ng/ml respectively. The median of biological parameters levels and standardized linear regression coefficients between serum ferritin

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Table1 Characteristic of gasoline workers

Characteristics	Median	Mean	Min-Max
Age (years old)	29.0	29.9	15.0 - 59.0
Income (baht)	6600.0	7065.1	5000.0 - 15000.0
Body Mass Index (kg/m^2)	22.06	23.2	16.3 - 41.2
Period of working time (years)	3.0	5.2	0.5 - 36.0
Working time per week (days)	6.0	6.2	4.0 - 7.0
Working time per day (hours)	10.0	10.4	6.0 - 12.0
	Percentage		
Smoking (%)	34.0	-	-
Alcohol drinking (%)	59.4	-	-
Coffee drinking (%)	62.3	-	-

Table 2 Linear regression coefficients in relation between laboratory values and serum ferritin

Parameters	Median N=106	Mean N=106	Min - Max	Standardized coefficients[a]	95% CI	*P*-value
Ferritin (ng/ml)	163.0	238.6	3.2 - 1917.0			
Hemoglobin (gm/dL)	14.1	14.0	6.1 - 17.3	-0.331	-0.004 to 0.000	0.015
Mean corpuscular volume (%)	82.8	82.0	57.2 - 98.7	-0.237	-0.016 to -0.001	0.070
WBC (X10^9/L)	7.5	7.9	4.7 - 13.1	0.195	0.000 to 0.003	0.144
BUN (mg%)	11.0	11.6	5.0 - 20.0	0.075	-0.002 to 0.004	0.565
Creatinine (mg%)	0.9	1.0	0.5 - 1.8	-0.220	0.000 to 0.000	0.109
SGOT (U/L)	22.0	26.2	1.0 - 150.0	0.587	0.028 to 0.058	<0.001
SGPT (U/L)	24.0	30.4	2.0 - 165.0	0.277	0.005 to 0.050	0.019
ALP (U/L)	64.0	71.2	26.0 - 298.0	0.168	-0.008 to 0.056	0.139
Serum Cholinesterase (U/L)	8603.5	9198.5	4656.0 - 6789.0	0.312	-0.874 to 2.570	0.756
Whole blood Cholinesterase (U/L)	5059.0	5096.5	3718.0 - 6789.0	0.119	-0.258 to 0.704	0.358

[a]Adjusted for age, income, body mass index, period of working time, working time per week and working time per day

(dependent variable) and biological parameters results (independent variables) adjusted for age, income, body mass index, period of working time, working time per week and working time per day of 106 gasoline workers are shown in Table 2. The results of this study indicate that serum ferritin was strongly related to SGOT *($p<0.001$)*, SGPT *($p<0.05$)* and inversely related to hemoglobin level *($p<0.05$).*

DISCUSSION

Ferritin is an iron-binding protein which is also present extracellularly within serum. It serves as an important clinical marker of iron status, especially in the liver [16]. The previous study found that 45.5% and 68.2% of gasoline workers had lower hemoglobin and an abnormal morphology of red blood cell, but higher SGOT, SGPT and ALP at 9.1%, 15.9%, and 38.6% respectively [12]. Moreover there was a significantly lower level of serum cholinesterase in gasoline worker than in control groups *($p<0.05$)* [13]. This may be caused by iron deficiency and some of the workers affected by liver function. The study found that 20.5% of workers had higher serum ferritin levels higher than normal, 20.0% in male and 23.0% in female workers. Only 4.7% of all workers had lower ferritin levels than normal. Normally, women have lower prevalence of iron overload-related disease than men, due to iron loss during menstruation [17, 18], and a decrease in ferritin level that occurs in erythropoietin [19]. The study showed that serum ferritin level of women workers were lower than those in men but the percentage of the number was not different between the two sexes, and none of the workers had serum ferritin less than 30 ng/ml.

In the present study, the relation between the serum ferritin level elevation and the biological parameters showed a strong positive relation (*$p<0.001$*) to liver functions. Increased SGOT were usually found in infected or damaged liver [20], such as chronic hepatitis [21] and cirrhosis [22]. As the result of this study, liver cell damage might be direct related to serum ferritin level [15]. It seems that liver dysfunction leads to elevated serum ferritin level by decreasing ferritin clearance, serum ferritin being cleared from blood circulation mainly in the liver. The serum ferritin level can be explained by direct and indirect affects. It is possible that the initial increase of serum ferritin is due to cell destruction and that the maintainance of high levels is due to a decrease in ferritin clearance. A recent population based hemochromatostasis screening study of nearly 30,000 white subjects showed that the use of

the single marker ferritin was a useful strategy. Serum ferritin higher than 1000 ng/ml detected only those who were at the highest risk for serious clinical manifestation such as cirrhosis [17, 23]. The present study found that 1.8% of workers had a serum ferritin higher than that level (1000 ng/ml). Therefore, they should be more biologically examined and followed up for liver disease diagnosis. For liver biopsy, it is necessary in some cases to assess the degree of iron overload and liver damage.

Moreover, serum ferritin was related to SGPT *($p<0.05$)*, SGPT being a liver enzyme made in the liver cells. If the liver cells become damaged, these enzymes can leak out. The SGPT level is more specific to the liver than the other enzymes because it is made mostly by the liver cells and not by other organs. A previous study revealed that serum ferritin and SGPT levels were correlated (*$r=0.374$, $P<.001$)* and had to be associated to the components of the metabolic syndrome [22, 24]. This study about serum cholinesterase didn't show any association with serum ferritin even though serum cholinesterase was significantly related to SGPT *($p<0.05$)*. It might be related to liver enzyme in a different pathway. These two SGOT and SGPT levels of most workers were in normal range, which is difficult to explain clearly, but it has to be considered for chronic liver disease in the future.

In general, both SGOT and SGPT are sensitive indicators of liver damage from different types of disease. In rare cases, higher than normal levels of these liver enzymes may have caused others than liver problems. The interpretation of elevated SGOT and SGPT levels depends upon the whole clinical picture. Some of these patients may have developed chronic liver disease, such as chronic hepatitis and cirrhosis, over the years.

In addition, serum ferritin was significantly *($p<0.05$*) inversely associated with hemoglobin level. The study found that 10.8% of the workers had lower hemoglobin levels than normal. But only 0.01% had hemoglobin level less than 10 g/dL. It may be conclude from the result, that all workers were not iron deficient because they had not serum ferritin less than 30 ng/ml. The possibility of serum ferritin elevation may be the result of a short half life of red blood cell and decrease clearance of ferritin in blood circulation caused by liver damage. The result of this study supported the previous study [25]. There were reports in patients with anemia, secondary to acute or chronic disease. A serum ferritin level greater than 100 ng/ml will likely be adequate to support hemoglobin regeneration [26] and every 1 g/dL decrease in hemoglobin level, as serum leads to an expectation, increase serum ferritin levels [27] by 20 ng/ml.

Lastly, even though mean of parameter levels of gasoline workers were in normal ranges, some serum ferritin levels showed a possible relation to chronic diseases. They may be an adverse affect of VOCs exposure in occupation and behavior of workers, such as cigarette smoking, alcohol drinking, nutrition and viral hepatitis. The limitation of this study was a cross-sectional analysis about the relationship between different variables (serum ferritin, and personal biological parameters) at a point in time. Unlike time series, cross-sectional analysis relates to how variables affect each other at the same time and period. Firstly, and as an advantage, the study found the associations between serum ferritin and SGOT, SGPT and hemoglobin (Hgb) referring to age, income, body mass index, period of working time, working time per week and working time per day which were multicollinearity. Secondly, the study could determine that SGOT affected more the outcome than Hgb and SGPT did respectively. Thirdly, the study predicted that serum cholinesterase might be related to serum ferritin if the study is performed in a larger number of gasoline workers. The evaluation of healthy workers with abnormal liver enzymes needs to be individualized. If alcohol or prescription drugs are responsible for the abnormal liver enzyme levels, stopping alcohol or the medication (under a doctor's supervision) may help. If abnormal liver enzymes persist despite abstinence from alcohol, a weight reduction and stopping certain suspected drugs, as well as blood tests, may support the treatment of liver diseases. The blood can be tested for the presence of the hepatitis B and C virus and their related antibodies. According to this study, serum ferritin could play a role as marker to predict iron overload and liver damage in gasoline workers group.

CONCLUSION

The present study has shown that the gasoline workers had a risk for liver cell damage factors with serum ferritin strongly related to SGOT *($p<0.001$)* and SGPT *($p<0.05$)*. In addition, serum ferritin was inversely related to hemoglobin level *($p<0.05$)* with a trend to a hematological disease such as mild anemia. It is difficult to explain precisely all the relationships because there were many possible confounders - disruptive factors - to interfere with the outcomes. Serum ferritin is a valuable tool for the evaluation of common disease states, such as iron deficiency anemia, and physical disease. For future ferritin research, it will be interesting to describe novel function of independency of iron storage. Future studies should direct the attention to all relations of elevated ferritin levels to liver and hematological parameters.

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