

Hepatic impairment among workers of furniture manufacture occupationally exposed to solvents in Egypt

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Background/aim

Organic solvents, which are used in many processes in furniture manufacture, are the most common chemicals that may be associated with liver injury. The present study aimed to determine the potential impact among workers exposed to mixtures of organic solvents on liver function tests.

Participants and methods

The present study included 63 workers occupationally exposed to organic solvents and 27 healthy individuals who served as a control group. The exposed group was divided into three subgroups according to the duration of employment: less than 10 years (G2), from 10 to 20 years (G3), and more than 20 years (G4) of employment. Six air samples were collected in the different production units using activated charcoal tubes according to a standard method developed by the National Institute of Occupational Safety and Health. Clinical data and demographic information were collected. Liver enzymes [alanine transaminase (ALT), aspartate transaminase (AST), γ -glutamyltransferase (GGT), alkaline phosphatase (ALP), and lactate dehydrogenase (LDH) activities] were measured in all participants.

Results

The mean level of organic solvents at air work place was below the maximum allowable limits according to international regulations and Egyptian Environmental Law 4. Serum ALT, AST, GGT, ALP, and LDH activities were significantly higher in exposed workers than in the controls. Serum AST and ALP activities were elevated in subgroups with duration of employment more than 10 years compared with the controls. Serum ALT, ALP, and LDH activities showed a significant positive correlation with the duration of employment.

Conclusion

The relationship between occupational exposure to organic solvents and hepatic injury was propounded, even though the exposure was below the permissible exposure limit. Serum ALT is a good biomarker of hepatocellular injury and a sensitive biomarker for exposure to solvents.

Keywords:

furniture manufacture, liver enzymes, organic solvents

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Introduction

Organic solvents and their vapors are a common part of our environment. They are used in industry for a variety of purposes. Organic solvents are used widely by furniture manufacturers in coatings sprayed onto wood, for thinning coatings, and for cleaning spraying equipment. Such solvents are volatile organic compounds (VOCs) emitted during their use, and they have the potential to damage both health and the environment [1]. Therefore, occupationally, organic solvents with strong toxicity are replaced with weaker ones. So far, studies on low-dose exposure to organic solvents are conflicting and difficult because the symptoms are slow to develop when exposure to organic solvents is in low concentrations [2].

Occupational exposure to solvents may lead to various injury and illness through inhalation of the toxic vapors and/or absorption of irritants through the

skin. The magnitude of hazards worsens in a confined area. Organic solvents are very toxic to the nervous system, liver, kidney, heart, and male reproductive hormones [3–8]. In general, the toxicity of solvents is related to their lipophilicity [9]. Exposure to significant concentrations can result in liver dysfunction, cell injury, and even organ failure [10].

In recent years, many investigators have concluded that occupational exposure to solvents may cause insidious damage to the liver; even exposure to a weaker solvent (hydrocarbons), but in large quantities, can cause acute liver necrosis, fatty liver, and hepatorenal syndrome. It

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was also reported that hepatorenal syndrome can be caused by habitual glue sniffing in toluene abuse [2].

The hepatotoxic effects of some of the solvents were recognized as early as 1887. Previous studies on the impact of organic solvents on liver function have mostly dealt with high doses, such as acute liver disease caused by dimethylformamide [11,12] and acute hepatitis caused by trichloroethylene [13]. So far, studies on low-dose exposure to organic solvents have shown no relationship with liver toxicity [14]. The clinical assessment of hepatotoxicity and industrial solvents must take into account synergism with medications as drugs of use and abuse such as ibuprofen and penicillin, alcohol, age, and nutrition [15].

For this reason, Brautbar and Williams [15] emphasized that cofactors play a critical role in toxicity from organic solvents. However, studies on the usefulness of traditional liver function tests in the detection of liver injury caused by a mixture of organic solvents are conflicting [16]. It is conceivable that the general picture of the effects will vary depending on the composition of the solvent mixture and the extent of exposure.

Clinical presentation of occupational liver disease may be acute/subacute or chronic, but is often insidious. Liver disease initially appears in the form of fatty liver. As it progresses, it deteriorates into hepatitis, liver cirrhosis, and liver cancer. Solvents may damage liver cells and liver transaminases may be used to monitor liver damage. Liver disease cannot be confirmed with a blood chemistry test, but clinically, alanine transaminase (ALT) is most commonly used as a biomarker of liver damage. In the liver function tests, ALT, aspartate transaminase (AST), and γ -glutamyltransferase (GGT) can be elevated by other organ damage than the liver [17]. Thus, to increase the sensitivity, different biochemical parameters of liver function should be measured [18], such as alkaline phosphatase (ALP), albumin, and lactate dehydrogenase (LDH).

The aim of the present study was to determine the potential impact of occupational exposure to mixtures of organic solvents on liver function tests.

Participants and methods

This study included 63 painting workers out of 1000 male workers in a furniture-manufacturing plant. They had worked in the painting and finishing processes for more than 2 consecutive years and were designated as the exposed group and therefore exposed directly or indirectly to a mixture of toluene,

styrene, and benzene at the work place. The exposed group was divided into three subgroups according to the duration of employment. Twenty-seven nonexposed male workers, who had worked outside the manufacturing building, were matched with the exposed workers for age, socioeconomic status, special habits, and duration of work, and were designated as the control group. An interview questionnaire was administered that was especially designed to cover present and past occupational histories as well as questions on manifestations suggestive of chronic solvents intoxications for both exposed and control groups.

Indoor air sampling

Six samples were collected in the different production units according to a standard method developed by the National Institute of Occupational Safety and Health using activated charcoal tubes [ORBO-32' Supelco, Bellefonte, PA USA 16823-0048, activated coconut charcoal (20/40)], at a flow rate of 200 ml/min, using an air sampling pump with electronic flow control (A.P. Buck Inc., Orlando, Florida, USA). The flow of the pump was calibrated using a Mini-Buck Optical Calibrator (A.P. Buck Inc.). After 4 h, the sampling was stopped by placing caps on both ends of the tubes. The tubes were covered in aluminum foil and stored at 4°C until analysis [19]. The laboratory analysis was carried out using gas chromatography (model 7890; Agilent Technology, Wilmington, DE 19808-1610 USA). The system was equipped with a flame ionization detector.

Blood sampling and biochemical methods

Five milliliters of blood was collected into a clean tube from each participant at 12:00–2:00 p.m. before the lunch break on the last day of the working week. Blood samples were left to clot for 20 min at 37°C and then centrifuged at 3000 rpm for 15 min. The sera were separated and stored at –20°C until measurement. ALT, AST, GGT, ALP, and LDH activities were measured using the Kinetic Kit (Randox Laboratories, 55 Diamond Road, Crumlin, County Antrim, BT29 4QY, United Kingdom) according to the methods of Glinghammar *et al.* [20], Goldman and Ausiello [21], Teitz [22], Englehardt *et al.* [23], and Weissshaar *et al.* [24], respectively.

Statistical analysis

The statistical package for the social sciences (SPSS, version 16.0; SPSS Inc., Chicago, Illinois, USA) program was used for analysis. Results are reported as mean $\pm$ SD. One-way ANOVA was performed for analysis of more than two variables, followed by a

post-hoc test for detection of significance. A simple linear correlation (Pearson's correlation) was used for quantitative data. Qualitative data were presented as frequencies (*n*) and percentages. Comparisons of quantitative data were performed using Student's *t*-test for data with a normal distribution. The level of significance was at less than 0.05.

Results

Identification of volatile organic compounds in the air at the work place

Analysis of VOCs in the air of the work place that were collected using activated charcoal tubes Table 1 confirmed that the workers were exposed to xylene, toluene, styrene, bromobenzene, and benzene; by contrast, trimethylbenzene, 1,2,3-trichlorobenzene, isopropyl, and 1,2,4-trichlorobenzene were found in traces. The concentrations of all VOCs detected were below the permissible exposure limit.

The demographic and other data of the exposed and controls are shown in Table 2. The mean age of the participants in the exposure and control groups was 39.2 ± 9.9 and 41.3 ± 15.1 years, respectively. The mean difference in age between the two groups was nonsignificant. The average years of employment were 13.74 ± 8.01 years. No statistically significant difference was found between exposed and control participants in terms of smoking habits ($P = 0.8$). When the protective measures were investigated, only 5% of the exposed workers were always using protective masks or gloves at work and the rest of them (95%) were rarely using or not using masks or gloves at all during work. Almost all participants reported that they had some type of medical complaints. The most frequently mentioned problems were with the eyes, skin mucous membrane irritations (56.6%), and musculoskeletal disorders, especially joint pain (53.3%).

Evaluation of liver functions

Liver function tests of the exposed workers and controls are shown in Table 3; these were statistically significantly increased in the means of ALT, AST, GGT, ALP, and LDH activities in occupationally exposed workers compared with the controls ($P < 0.0001$, <0.001 , <0.0006 , <0.002 , and <0.0001 , respectively). No statistically significant differences were found between subgroup G2 and controls in serum AST, ALP, and GGT. There was a statistically significant increase in the means of AST and ALP activities in exposed workers with a duration of employment longer 10 years (G3 and G4) compared with controls.

Table 3 shows the correlation between duration of employment and liver function tests in exposed workers. Serum ALT, ALP, and LDH showed a significant positive correlation with the duration of employment ($P < 0.024$, <0.0001 , and <0.029 , respectively), whereas the correlation of serum AST and GGT with the duration of employment was not significant ($P < 0.214$ and <0.055 , respectively) (Table 4).

Discussion

Exposure to mixtures of organic solvent is more commonly found rather than exposure to a single one. The additive effect of a mixture of organic solvents causes increased hepatotoxicity, even if the concentration of the solvents is below the environmentally permissible concentrations [25]. As shown in this study, workers engaged in painting and varnishing sectors in the furniture enterprise are exposed to a mixture of volatile organic solvents, which were, according to air analysis of the work place, below the threshold value of exposure permissible limits. Notably, it was unveiled that furniture workers in those sectors had 6.95 and 1.64 times of toluene and benzene, respectively, higher than those of the

Table 1 Concentration of different volatile organic compounds (mg/m³) in the air at the work place

VOCs	Mean concentration	OSHA PEL TWA	NIOSH REL TWA	MAC	ACGIH 2004 TLV TWA
Toluene	151	760	375	192	192
Xylene	174	435	435	334	345
Benzene	1.4	3.19	3.19	1.6	3.2
<i>n</i> -Butyl benzene	10.28	NA	NA	70.5	NA
Styrene	126.5	420	215	126.5	85
Trimethylbenzene	1.4	NA	125	NA	NA
1,2,3-Trichlorobenzene	0.1	NA	NA	0.1	NA
Isopropyl	1.71	980	980	983	400
Bromobenzene	49.14	NA	NA	NA	NA
1,2,4-Trichlorobenzene	0.09	NA	NA	NA	NA

Source: ICSC (<http://www.cdc.gov>); ACGIH, American Conference of Industrial Hygienists; MAC, maximum allowable concentrations according to Egyptian Environmental Law 4; NIOSH, National Institute of Occupational Safety and Health; OSHA, Occupational Safety and Health Administration of the US; PEL, permissible exposure limits by US laws; REL, recommended exposure limits; TLV, threshold limit value; TWA, time-weighted average for 8 h shift; VOC, volatile organic compound.

non-exposed group, and workers who worked for more than 8 h/day had higher blood toluene and benzene levels [26].

In our study, the biochemical measurements were selected to assess hepatic injury associated with necrosis including the serum hepatic transaminases ALT and AST and hepatic cholestasis including ALP and GGT [27,28].

ALT is an enzyme involved in the transfer of an amino group from alanine and present in the cytoplasm. ALT is found in various tissues, but is most commonly associated with the liver. Therefore, ALT is a good biomarker of hepatocellular injury [29]. AST is an enzyme involved in the transfer of an amino group from aspartate. More than 80% of AST is present in the mitochondria and the remaining 20% of AST is present in the cytoplasm. Thus, cytosolic AST immediately appears in the blood from an injured cell, but mitochondrial AST remains in the core regions of an injured cell. Thus, mitochondrial AST in the blood reflects the more severe cell damage or necrosis [30]. In case of alcoholic hepatitis, mainly the mitochondria are damaged. Thus, AST increases more than ALT [30], which is not obvious in our study. It is generally accepted that increased cytosolic enzyme in the blood occurs secondary to cell membrane damage or cell necrosis [31]. Therefore, increased AST and ALT are biomarkers of hepatic injury rather than hepatic dysfunction [29].

Table 2 Demographic characteristics of healthy participants and workers exposed to solvents under investigation

Parameters	Control (N = 27)	Exposed (N = 63)	P-value
Age (mean $\pm$ SD) (years)	41.3 $\pm$ 15.1	39.2 $\pm$ 9.9	0.458
Duration of employment (mean $\pm$ SD) (years)	—	13.71 $\pm$ 8.01	—
Nonsmoker [n (%)]	20 (74.1)	45 (71.4)	0.8
Smoker [n (%)]	7 (25.9)	18 (28.6)	
Using personal protective equipment [n (%)]			
No	—	42 (66.66)	—
Yes	—	21 (33.33)	—
Always	—	3 (14.29)	—
Rarely	—	18 (85.71)	—

The present study showed that the mean ALT and AST serum activities were significantly elevated in exposed participants compared with controls. Similarly, many studies have shown increased levels of liver transaminases in workers exposed to a mixture of aromatic solvents [32–36]. Emara *et al.* [37] proved that there was deterioration in hepatic functions among 74 spray painters exposed to more than 20 different solvents, especially transaminases. Metwally and El-Shabrawy [36] found that the mean levels of ALT and AST were significantly higher among the car-spraying painting workers compared with controls. Similar results were reported by Hussein *et al.* [33] among shoemakers. Iavicoli *et al.* [38] found higher hepatic transaminases in workers exposed to low doses of isopropanol. Also, Caciari *et al.* [32] found the same changes in transaminases among a large group of workers exposed to organic solvents. Our results were not in agreement with those of Ukai *et al.* [14] and Amr *et al.* [39], who reported that the liver function tests in their studies did not show any exposure-related abnormality, and Fernández-D'Pool and Oroño-Osorio [25] attributed the changes, if present, to obesity and alcohol consumption, and not to the occupational factors of the plant that they studied.

Kaukiainen *et al.* [34] reported a positive correlation between serum ALT and AST and cumulative solvent exposure for 5 years in a study of 29 solvent-exposed workers and 19 controls; also, Brodtkin *et al.* [40] reported evidence for diminished hepatic clearance in workers exposed to styrene in addition to a significant linear association between the hepatic transaminases ALT and AST and exposure to styrene, which is consistent with mild hepatic injury. In addition, Mohammadi *et al.* [41] found a significant relationship between ALP level and exposure to a mixture of organic solvents. In our study, we found the same positive correlation for ALT, ALP, and LDH and the duration of employment. Our result confirmed that ALT is a good biomarker of hepatocellular injury and a sensitive biomarker for exposure to solvents in the study groups as it showed a significant gradual increase in all the exposed groups (G2, G3, and G4), whereas the AST showed an increase only in the groups of workers with more than 10 years of exposure (G3 and G4) than the control group.

Table 3 Liver function tests of controls and workers exposed to organic solvents

Liver function tests	Controls (G1) (n = 27)	G2 (n = 24)	G3 (n = 22)	G4 (n = 17)	Total (n = 63)
ALT (U/l)	22.74 $\pm$ 5.61	29.37 $\pm$ 8.05*	30.59 $\pm$ 8.25*	34.70 $\pm$ 5.417*	31.23 $\pm$ 7.71*
AST (U/l)	21.40 $\pm$ 3.93	25.29 $\pm$ 8.90	26.72 $\pm$ 7.27*	28.41 $\pm$ 5.85*	26.74 $\pm$ 7.57*
GGT (U/l)	15.70 $\pm$ 3.07	16.75 $\pm$ 4.52	20.09 $\pm$ 4.98*	19.05 $\pm$ 4.60	18.53 $\pm$ 4.86*
ALP (U/l)	168.52 $\pm$ 5.83	164.92 $\pm$ 29.74	213.82 $\pm$ 35.62*	224.5 $\pm$ 32.85*	198.08 $\pm$ 5.65*
LDH (U/l)	240.44 $\pm$ 21.93	311.75 $\pm$ 62.2*	332.06 $\pm$ 63.53*	351.06 $\pm$ 68.37*	329.46 $\pm$ 65.22*

All data expressed as mean $\pm$ SD; ALP, alkaline phosphatase; ALT, alanine transaminase; AST, aspartate transaminase; GGT, γ -glutamyltransferase; LDH, lactate dehydrogenase; * P < 0.05, significant difference compared with the control group.

Table 4 Correlation coefficient between duration of employment and liver function tests among the exposed workers

Liver function tests	Duration of employment (years)	
	<i>r</i>	<i>P</i> -value
ALT (U/l)	0.284*	<0.024
AST (U/l)	0.159	0.214
GGT (U/l)	0.243	0.055
ALP (U/l)	0.641**	<0.0001
LDH (U/l)	0.276*	<0.029

ALP, alkaline phosphatase; ALT, alanine transaminase; AST, aspartate transaminase; GGT, γ -glutamyltransferase;

LDH, lactate dehydrogenase; **Significant at $P < 0.01$;

*Significant at $P < 0.05$.

GGT is a membrane-bound enzyme found in the kidneys and liver. Renal GGT is excreted into the urine, not the blood. Meanwhile, hepatic GGT has direct access to the blood. Hence, most of the serum GGT activity in the blood is from the liver. GGT is released into blood by cellular injury, cholestasis, or overproduction, which is induced by medication [38]. Elevated GGT alone may be found in chronic alcoholics. This finding is not obvious in our study. Lee *et al.* [42] suggested that GGT can be used not only as a liver function index and biomarker of alcohol intake and of oxidative stress. In the present study, tests of hepatic cholestasis used (GGT and ALP) showed significant differences between the two groups studied (the exposed and the control), which is consistent with several studies on workers exposed to organic solvents, which have shown increased levels of liver transaminases and GGT, which indicated that hepatic cholestasis and necrosis were two common exposure effects [33,43,44]. Meanwhile, the two cross-sectional studies of Brodtkin *et al.* [40] in workers exposed to lower levels of styrene have shown increased levels of direct bilirubin and ALP compared with the control groups, but no increase in transaminases, which meant mild hepatic disorder without significant hepatic parenchymal necrosis [40]. Chen *et al.*'s [45] study observed an increased activity of GGT only and its activity was related to the intensity of exposure to a mixture of organic solvents as xylene and toluene were the most common contaminants in the air samples of their study [45]. The results of Mohammadi *et al.*'s [41] study were consistent with ours in terms of the significance of the ALP difference between the exposed and the control group.

Dere and Ari [46] reported that benzene inhalation in rats caused a significant increase in LDH, ALP, ALT, and AST activities in the serum of exposed rats compared with the control groups, which is in accordance with our results; the increasing in LDH activities in the exposed group may have been because of the hepatocellular necrosis leading to leakage of the enzyme into the blood stream. In general, the

discrepancy between various studies could be because of the difference in the sample size, study method, type of the solvent studied, exposure intensity, and liver tests studied.

In conclusion, the relationship between the occupational exposure to organic solvents and hepatic injury was propounded, even if the exposure was below permissible exposure limit. Serum ALT increased gradually and correlated with the duration of employment, which indicated that serum ALT is a good biomarker of hepatocellular injury and a sensitive biomarker for exposure to solvents.

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Conflicts of interest

There are no conflicts of interest.

References

- Lim SK, Shin HS, Yoon KS, Kwack SJ, Um YM, Hyeon JH, *et al.* Risk assessment of volatile organic compounds benzene, toluene, ethylbenzene, and xylene (BTEX) in consumer products. *J Toxicol Environ Health A* 2014; 77:1502–1521.
- Park CK, Kwon KT, Lee DS, Jo CM, Tak WY, Kweon YO, *et al.* A case of toxic hepatitis induced by habitual glue sniffing. *Taehan Kan Hakhoe Chi* 2003; 9:332–336.
- Eldesouki MA, Sharaf NE, Abdel Shakour AA, Mohamed MS, Hussein AS, Hasani IW. Study of the effect of occupational exposure to volatile organic compounds (VOC's) on male reproductive hormones. *World J Med Sci* 2013; 8:6–12.
- Kim S. The reduction of formaldehyde and VOCs emission from wood-based flooring by green adhesive using cashew nut shell liquid (CNSL). *J Hazard Mater* 2010; 182:919–922.
- Hegazy NM, Abdel Gawad NB, Metwally FM, Ahmed HH, Abdel Raouf ER, Abraham KS, Sharaf NE. Neurotoxic effects of organic solvents in exposed workers: altered expression of some biochemical markers. *New York Sci J* 2010; 3:171–176.
- Voss JU, Roller M, Brinkmann E, Mangelsdorf I. Nephrotoxicity of organic solvents: biomarkers for early detection. *Int Arch Occup Environ Health* 2005; 78:475–485.
- Filley CM, Halliday W, Kleinschmidt-DeMasters BK. The effects of toluene on the central nervous system. *J Neuropathol Exp Neurol* 2004; 63:1–12.
- Tomei F, Giuntoli P, Biagi M, Baccolo TP, Tomao E, Rosati MV. Liver damage among shoe repairers. *Am J Ind Med* 1999; 36:541–547.
- Winder C, N. Stacey. Toxicity of organic solvents, in *Occupational Toxicology*, Second edition, Winder and Stacey (ed). CRC press, Boca Raton London New York Washington, D.C., 2005; 14:364–388.
- Klaassen CD. *Casarett and Doull's toxicology: the basic science of poisons*. 7th ed. New York, USA: McGraw-Hill; 2008. 1310.
- Kang SK, Jang JY, Rhee KY, Chung HK. A study on the liver dysfunction due to dimethylformamide. *Korean J Occup Environ Med* 1991; 25:58–64.
- Heo JH, Lee KL, Han SG, Kim HJ, Pai YM, Whang YH, *et al.* A case of fulminant hepatitis due to dimethylformamide. *Korean J Gastroenterol* 1999; 34:547–550.
- Chae HJ, Lee SK, Lee KJ, Kim JY, Lee SC, Shin DH, *et al.* Exfoliative dermatitis and toxic hepatitis associated with occupational exposure to trichloroethylene. *Korean J Occup Environ Med* 2003; 15:111–117.

- 14 Ukai H, Takada S, Inui S, Imai Y, Kawai T, Shimbo S, Ikeda M. Occupational exposure to solvent mixtures: effects on health and metabolism. *Occup Environ Med* 1994; 51:523–529.
- 15 Brautbar N, Williams J II. Industrial solvents and liver toxicity: risk assessment, risk factors and mechanisms. *Int J Hyg Environ Health* 2002; 205:479–491.
- 16 Nunes de Paiva MJ, Pereira Bastos de Siqueira ME. Increased serum bile acids as a possible biomarker of hepatotoxicity in Brazilian workers exposed to solvents in car repainting shops. *Biomarkers* 2005; 10:456–463.
- 17 Green RM, Flamm S. AGA technical review on the evaluation of liver chemistry test. *Gastroenterology* 2002; 123:1367–1384.
- 18 Ministry of Employment and Labor. Report on worker's health examination result; 2009. Available: http://www.moel.go.kr/view.jsp?cate=3&sec=2&mode=view&bbs_cd=5&bbs_cd=107&state=A&seq=1301623504781 [Last accessed on 2012 Aug 1].
- 19 Scheepers PT, Konings J, Demirel G, Gaga EO, Anzion R, Peer PG, *et al.* Determination of exposure to benzene, toluene and xylenes in Turkish primary school children by analysis of breath and by environmental passive sampling. *Sci Total Environ* 2010; 408:4863–4870.
- 20 Glinghammar B, Rafter I, Lindström AK, Hedberg JJ, Andersson HB, Lindblom P, *et al.* Detection of the mitochondrial and catalytically active alanine aminotransferase in human tissues and plasma. *Int J Mol Med* 2009; 23:621–631.
- 21 Goldman L, Ausiello D, editors. *Cecil medicine (chapter 15)*. 23rd ed. Philadelphia, PA: Saunders Elsevier; 2007.
- 22 Teitz NN. *Fundamental of clinical chemistry*. 3rd ed. Philadelphia: WB Saunders Co.; 1987. 391.
- 23 Englehardt A. Measurement of alkaline phosphatase. *Aerztl Labor* 1970; 16:42.
- 24 Weisshaar HD, Weisshaar HD, Prasad MC, Parker RS. Estimation of lactate dehydrogenase in serum/plasma. *Med Welt* 1975; 26:387.
- 25 Fernández-D'Pool J, Oroño-Osorio A. Liver function of workers occupationally exposed to mixed organic solvents in a petrochemical industry. *Invest Clin* 2001; 42:87–106.
- 26 Mandiracioglu A, Akgur S, Kocabiyyik N, Sener U. Evaluation of neuropsychological symptoms and exposure to benzene, toluene and xylene among two different furniture worker groups in Izmir. *Toxicol Ind Health* 2011; 27:802–809.
- 27 Stolz A, Kaplowitz N. Biochemical tests for liver disease. In: Zakim D, Boyer TD, editors. *Hepatology*. Philadelphia: WB Saunders; 1990. 637–657.
- 28 Seetharam S, Sussman NL, Komoda T, Alpers DH. The mechanism of elevated alkaline phosphatase activity after bile duct ligation in the rat. *Hepatology* 1986; 6:374–380.
- 29 Kim YJ. Interpretation of liver function tests. *Korean J Gastroenterol* 2008; 51:219–224.
- 30 Kamiike W, Fujikawa M, Sumimura J, Miyata M, Kawashima Y, Wada H, Tagawa K. Differential patterns of leakage of cytosolic and mitochondrial enzymes. *Clin Chim Acta* 1989; 185:265–270.
- 31 Solter PF. Clinical pathology approaches to hepatic injury. *Toxicol Pathol* 2005; 33:9–16.
- 32 Caciari T, Casale T, Pimpinella B, Montuori L, Trovè L, Tomei G, *et al.* Exposure to solvents in health care workers: assessment of the hepatic effects. *Ann Ig* 2013; 25:125–136.
- 33 Hussein AS, Mohgah S, Abdalla H, Jihan S. Antioxidants in shoe-makers exposed to organic solvents. *J Appl Sci Res* 2008; 4:1107–1117.
- 34 Kaukiainen A, Riala R, Martikainen R, Reijula K, Riihimäki H, Tammilehto L. Respiratory symptoms and diseases among construction painters. *Int Arch Occup Environ Health* 2005; 78:452–458.
- 35 Lundberg I, Hogstedt C, Linden C, Nise G. Organic solvents and related compounds. In: Rosenstock L, Cullen M editors. *Textbook of clinical occupational and environmental medicine*. 2nd ed. Philadelphia: Elsevier-Saunders Press; 2005. 991.
- 36 Metwally FM, El-Shabrawy IM. Biochemical alteration of liver and kidney functions among spray painters. *Kasr El Aini Med J* 2000; 6:141.
- 37 Emara A, El-Safty A, Siha M. Health hazards among spray painters. *Egypt J Occup Med* 1996; 20:7–13.
- 38 Iavicoli I, Fontana L, Iavicoli S. Modifications of hepatic transaminases in workers exposed to low doses of isopropanol. *G Ital Med Lav Ergon* 2007; 29(Suppl): 271–272.
- 39 Amr MM, Abbas EZ, Gaballah IF, Farahat SA, Ahmed MH. Health profile of workers in the paint industry. *Egypt J Occup Med* 2001; 25:71–89.
- 40 Brodtkin CA, Moon JD, Camp J, Echeverria D, Redlich CA, Willson RA, Checkoway H. Serum hepatic biochemical activity in two populations of workers exposed to styrene. *Occup Environ Med* 2001; 58:95–102.
- 41 Mohammadi S, Mehrparvar AH, Labbafinejad Y, Attarchi MS. The effect of exposure to a mixture of organic solvents on liver enzymes in an auto manufacturing plant. *J Public Health (Bangkok)* 2010; 18:553–557.
- 42 Lee DH, Blomhoff R, Jacobs DR Jr. Is serum gamma glutamyltransferase a marker of oxidative stress?. *Free Radic Res* 2004; 38:535–539.
- 43 Tomenson JA, Baron CE, O'Sullivan JJ, Edwards JC, Stonard MD, Walker RJ, Fearnley DM. Hepatic function in workers occupationally exposed to carbon tetrachloride. *Occup Environ Med* 1995; 52:508–514.
- 44 Ann CY, Lee KJ, Park JB, Jang JY, Kim MJ. The association of exposure to organic solvents with liver function. *Korean J Occup Environ Med* 2001; 13:64–74.
- 45 Chen JD, Wang JD, Jang JP, Chen YY. Exposure to mixtures of solvents among paint workers and biochemical alteration of liver function. *Br J Ind Med* 1991; 48:696–701.
- 46 Dere E, Ari F. Effect of benzene on liver functions in rats (*Rattus norvegicus*). *Environ Monit Assess* 2009; 154:23–27.