## **Summary**

Organic solvents are among the most widely used chemicals in several industries. Exposure to solvents occurs in a variety of workplace and community settings. Occupational exposure to mixed organic solvents is more common than to a particular solvent. Organic solvents are still an important occupational health problem due to their widespread usage. Long term exposure has adverse effects on human health.

The most common chemicals known to cause liver injury are the organic solvents. Naturally, the additive effect of a mixture of organic solvents causes increased hepatotoxicity.

Some studies have investigated the relationship between liver injury and combined exposure to multiple solvents present in paints and glues. In order to detect signs of dysfunction, several indices have been suggested, but they are not sufficiently sensitive as indices of early modifications and they are of limited use for screening workers exposed to solvents for which overt hepatotoxicity is not a major outcome.

This study was designed aiming at, evaluating the potential hepatotoxic effects resulting from occupational exposure to organic solvents by liver function tests, trying to define an early marker of hepatic impairment in the early reversible stage and comparing serum bile acids as a marker of hepatic impairment with Gamma-Glutamyl Transferase. Also, we aimed at studying the effect of exposure to organic solvents on ventilatory function.

So, we conducted a cross-sectional study on subjects occupationally exposed to organic solvents who were randomly selected from Pachin factory for paints and inks manufacturing. The studied population consisted of 2 groups, 57 exposed subjects and 59 randomly selected male volunteers as controls who had never been occupationally exposed to any solvent.

They were interviewed with the use of a designed questionnaire comprised personal data, smoking habits, gastrointestinal and respiratory manifestations, medical history and medications.

Each person was subjected to measurement of weight, height to calculate body mass index, general examination and full clinical examination. Blood samples for laboratory investigations were collected.

The following investigations were done, assessment of some classical biochemical parameters of liver function, like ALT, AST, ALP, total and direct bilirubin and GGT. In addition to assessment of serum bile acid which was suggested as a sensitive indicator of hepatotoxicity than the conventional measures.

Also they were investigated for their pulmonary functions including Forced Vital Capacity (FVC in liters), Forced Expiratory Volume in first second (FEV1 in litres), FEV1/FVC ratio (%), Peak Expiratory Flow (PEF in litres/min) and forced expiratory flow (FEF).

Mean values of Gamma –glutamyl transferase and serum bile acids were statistically significantly higher among exposed groups (26.7±24.8 and 50.2±47.9) than controls (24.4±11.9 and 5.4±2.7) respectively. Among the measured

parameters of liver function, SBA was the most frequently altered parameter in exposed workers with (87.7%) of them showing results above the upper reference limit followed by GGT (10.5%). But GGT sensitivity is denied because it may be a form of enzyme induction rather than a marker.

Regarding the ventilatory functions tests, it was revealed that the mean values of FEV1 and FEV1/FVC ratio in exposed subjects (80.30±17.79 and 98.83 ±16.89) were lower in comparison with those of the controls (89.97±22.48 and 111.84±14.24) respectively. Also, we found that (50.9%) of exposed had FEV1 impairment, (17.5%) had FEV1/FVC ratio impairment and (68.4%) had pulmonary obstruction.

The exposed subjects were classified according to the intensity of solvents exposure by estimating lifetime hydrocarbon exposure score (HES) into high exposure group (HEG) and low exposure group (LEG). We found that, the mean levels of GGT and SBA were much higher in HEG (30.25  $\pm$  25.9 and 63.7  $\pm$  49.5) than that in LEG (17.7  $\pm$  13.05 and 15.5  $\pm$  15.4) respectively. Our results also indicated that the FEV1 and FEV1/FVC ratio were altered in high exposure group than in low exposure group. Also, (85.4%) of HEG versus (25%) of LEG suffered from pulmonary obstruction.

Moreover, the exposed subjects were categorized according to the duration of exposure; SBA mean level was the only parameter that differs in each of the compared groups ( $63.8 \pm 47.4$  and  $24.8 \pm 38.3$ ) respectively. We found that, the workers with longer duration of exposure to organic solvents were more affected as regards FEV1/FVC ratio impairment than those with shorter duration of exposure. Also, pulmonary obstruction was more in group 1 than group 2.

Results also revealed that serum bile acids correlated positively with duration ( $\mathbf{r}=0.393$ ) and with level of exposure to organic solvents ( $\mathbf{r}=0.332$ ).

So, our work emphasis the hypothesis, those serum bile acids are more sensitive as markers for liver affection even on short exposure duration and at low levels of exposure.

So in conclusion, SBA level could be considered as a valid, reliable biomarker of early, subtle liver affection by industrial chemicals. So, we suggest that, it should be used as an index in the biological monitoring of workers exposed to hepatotoxic risks in preemployment examination and during their periodic examination not only as research tool.

Hence, it could be also concluded that that the longer the duration and the heavier intensity of exposure to organic solvents, the more the decline in the spirometric parameters especially FEV1. This adds to the growing of evidence of adverse respiratory effects of occupational solvent exposure. We stress on the necessity of preventive measures for solvent exposed workers to avoid the possible adverse effects of organic solvents on respiratory system.