

# Research Paper: Occupational Exposure to Paving Asphalt Fumes' Impact on Liver and Kidney Function Test Parameters



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## ABSTRACT

**Background:** Asphalt is a mixture of aliphatic and aromatic hydrocarbons. It also contains different kinds of heavy metals. Hot mix asphalt emits hazardous volatile substances. Asphalt is used in many industries, causing serious adverse health effects for workers. Therefore, investigation of the health status of workers is of crucial importance. The present study aimed to assess the impact of asphalt vapor on hepatic and renal function tests parameters and the clinical parameters in road paving workers compared to healthy subjects.

**Methods:** In a cross-sectional study, 41 road asphalt paving workers and 120 healthy non-exposed subjects were selected. The serum enzymes of Aspartate Aminotransferase (AST), Alanine Aminotransferase (ALT), Alkaline Phosphatase (ALP), total bilirubin, triglyceride, urea, and creatinine levels were assessed using diagnostic kits. A medical practitioner examined all subjects for any possible medical condition.

**Results:** Liver and kidney function test parameters were significantly higher in road asphalt paving workers compared to their healthy counterparts ( $P < 0.05$  for all parameters). About 63% of workers exposed to asphalt fumes for more than 10 years showed cardiac, pulmonary, and metabolic complications.

**Conclusion:** Significant elevations in liver and kidney function test parameters suggest that exposure to asphalt fumes is associated with hepatic and renal dysfunction in asphalt-exposed workers.

## 1. Introduction



Asphalt workers are exposed to different hazardous substances emitted from hot mix asphalt. This issue raises awareness and captures the attention of the health

of workers involved in the asphalt-associated industries. Asphalt is a product of crude petroleum distillation at atmospheric or under reduced pressure [1]. It is a mixture of bitumen and other binders, fillers, different proportions of mineral matter, modulators, and modifiers. These compounds include antioxidants, anticorrosive agents, fibers,

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plastic rubbers, and other waste materials [2]. Asphalt contains about 7% to 10% bitumen and is heated up to 230°C-250°C to be processed for working. Bitumen is widely used in the construction industry for roofing, road paving, and sealing cracks and joints in pavements [3]. Bitumen contains carbon, hydrogen, nitrogen, sulfur, and heavy metals [4]. During the hot application of bitumen, volatile and the most hazardous substances are released. They comprise aliphatic hydrocarbons and Polycyclic Aromatic Hydrocarbons (PAHs) [5].

The annual production of bitumen and asphalt in industrialized countries is about 60 and 700 million tons, respectively. The National Institute for Occupational Safety and Health (NIOSH) cited scientific evidence concerning the health issues of asphalt based on data from animal and human studies [1]. Also, International Agency for Research on Cancer (IARC, Occupational exposures to bitumen and their emissions 2011) classified occupational asphalt exposure during road paving as group 2B (possibly carcinogenic to humans) [6, 7]. Asphalt production and processing are among the major anthropogenic sources of PAHs [8]. PAHs are carcinogenic compounds at relatively low concentrations and are categorized as the most atmospheric pollutants [9, 10]. These substances are produced during incomplete combustion or pyrolysis of organic substances or petroleum [9]. The major routes for PAHs absorption are ingestion, inhalation, and dermal contact [10]. Because of their lipophilic nature, they are rapidly and widely distributed in the body and metabolized in the liver. Petrol fumes containing hydrocarbons have been reported to enhance oxidative stress in many cells [11]. It was indicated that some PAHs could be involved in producing reactive oxygen species (ROS) [12].

Hydrocarbons are converted to epoxides via metabolic processes. Epoxides are highly reactive substances and lead to cytotoxic effects due to binding to hepatic microsomal, renal proteins, and nucleic acids [11]. Also, nanoparticles are used in asphalt for high-performance and long-lasting effects [13]. Asphalt, bitumen, and their mineral fillers are among the sources of heavy metals such as Zinc (Zn), Copper (Cu), Nickel (Ni), Chromium (Cr), Lead (Pb), and Cadmium (Cd) in the environment [12]. The role of high levels of hepatic heavy metals such as Cd on liver enzymes level has been investigated in patients with hepatitis [14]. The effect of natural and synthetic chemicals on liver enzyme disruption was confirmed by other colleagues [15]. Petroleum products impair normal liver function. Serum enzymes such as Aspartate Aminotransferase (AST), Alanine Aminotransferase (ALT), and Alkaline Phosphatase (ALP) are

good indicators of liver function [11]. The previous investigation on workers exposed to bitumen confirmed urinary PAHs metabolites in higher concentrations compared to the control group [5]. Elevated levels of GGT and ALT enzymes were reported in construction workers in previous studies [16]. In their research on asphalt workers, Neghab et al. found that exposure to asphalt can be hepatotoxic, nephrotoxic, and hematotoxic [17].

Researchers have focused on assessing the organ toxicity of different chemicals in humans. Nowadays, the principal toxicological concern has been the potential organ toxicity of asphalt fumes. There are reports that ALT, AST, and ALP are used as biomarkers indicating hepatobiliary and renal disorders in occupational health surveillance. With the increasing interest of the general public and regulatory authorities over the occupational health and potential toxicity of air contaminants in workers dealing with hazardous substances, this research study was conducted to know the effect of bitumen vapor on liver enzymes activity, total bilirubin, plasma urea, and creatinine levels in road asphalt paving workers.

## 2. Materials and Methods

### Study population

The study has a cross-sectional design. The study samples included male asphalt exposed cases and non-exposed controls. Asphalt paving crews were pave operators, screedmen, and rakers. Forty-one road asphalt paving workers with at least five years (6 h/d, 5 d/wk) history of continuous exposure to asphalt and bitumen fumes were selected as the case group. Also, 120 non-exposed subjects were randomly chosen from cases with no history of exposure to asphalt or bitumen fumes from healthy subjects with other occupations without exposure to asphalt and bitumen. Potential confounders such as age, smoking habit, Body Mass Index (BMI), daily diet, physical activity, and daily workload were tested and adjusted one by one using regression analysis. The research was conducted with particular attention to personal traits. The previous history of diseases or drug use were assessed during face-to-face interviews. All cases with a history of drug use or medical complications were excluded from the study. All study subjects provided informed consent before sample collection.

### Sample collection

A total of 41 blood samples (10 mL each) were collected from antecubital veins of road asphalt paving workers and also 120 blood samples from the non-exposed con-

trol group in a similar way. Blood samples were transferred to test tubes and allowed to clot for 30 min before being centrifuged at 3500 rpm for 15 min. The serum samples were used for biochemical parameters analysis.

### Medical examination

Along with blood and urine sample collection, the interviews were conducted, and a physician medically examined all cases. Also, documents involving previous medical history, diagnostic images/photographs, and laboratory results were systematically inspected.

### Liver and kidney function tests assessment

Biochemical analyses were carried out for the determination of liver and kidney function test parameters, including estimation of ALT, AST, ALP, total bilirubin, urea, and creatinine in serum samples using analytical grade diagnostic kits (Liquicomfort Plus, PARS AZ-MUN) and AutoAnalyzer (model Hitachi 917, Japan).

### Statistical procedures

All data were analyzed in SPSS v. 13.0 software, SPSS Inc., Chicago, IL. All data were expressed as Mean $\pm$ SD. The Kolmogorov-Smirnov test was used for testing the normality of enzymes activities distribution in the case and control groups. The Student t test was used to evaluate the mean values of the measured parameters in the asphalt-exposed group compared to the corresponding non-exposed group. Values were regarded as significantly different at  $P<0.05$ .

## 3. Results

To evaluate the effect of asphalt and bitumen fumes on the liver and kidney, we measured liver function tests and also plasma urea and creatinine levels in road asphalt paving workers compared to the control group. Table 1 presents the results of the hepatic and renal markers in road asphalt paving workers and the control group. Table 1 summarizes serum levels of liver function test parameters, plasma urea, and creatinine levels in two groups. A glance at the obtained results shows that the mean values for studied liver function tests and creatinine and urea were significantly higher in road asphalt paving workers than in the control group ( $P<0.05$ ). Mean $\pm$ SD ages of the case and control groups were  $39.2\pm10.41$  and  $40.02\pm10.70$  years, respectively. Mean $\pm$ SD Body Mass Index (BMI) of the case and control groups were  $25.96\pm1.88$  and  $25.39\pm1.9$  kg/m<sup>2</sup>, respectively. Confounders such as age and BMI were equally distributed over both exposed and non-exposed groups due to randomization. It should be noted that there were no significant differences between the case and control groups regarding BMI and age parameters ( $P=0.1748$  and  $P=0.7259$ , respectively).

Clinical investigation of cases showed that 22 patients (53.7%) suffered from medical complications. Frequencies of common medical complications are presented in Table 2. It is worth noting that all cases with medical complications had exposure to asphalt fumes for more than 10 years. Table 3 presents the length of exposure to asphalt fumes.

**Table 1.** Normal ranges and Mean $\pm$ SD of liver and kidney function parameters assessed in road asphalt paving workers compared

Parameter	Mean $\pm$ SD		P	Normal Ranges and Units of Parameters
	Non-exposed Control Group (n=120)	Asphalt-exposed Group (n=41)		Range
Total bilirubin	0.74 $\pm$ 0.32	1.47 $\pm$ 0.56	0.0001	0.1-1.2 mg/dL
ALT	20.54 $\pm$ 4.63	31.07 $\pm$ 17.65	0.0001	12-33 U/L
AST	21.63 $\pm$ 5.06	31.10 $\pm$ 14.99	0.0001	11-35 U/L
ALP	127.27 $\pm$ 41.57	208.71 $\pm$ 75.61	0.0001	80-298 U/L
TG	120.39 $\pm$ 19.35	193.76 $\pm$ 62.93	0.0001	72-150 mg/dL
Urea	24.39 $\pm$ 7.64	31.51 $\pm$ 7.92	0.0001	12-40 mg/dL
Creatinine	0.83 $\pm$ 1.99	1.01 $\pm$ 0.21	0.0002	0.5-1.3 mg/dL

ALT: Alanine Aminotransferase; AST: Aspartate Aminotransferase; ALP: Alkaline Phosphatase; TG: Triglyceride.

**Table 2.** Frequency of medical complications in road asphalt paving workers

Complication	No. (%)
Cardiovascular system	
Dysrhythmia	
Hypertension	12 (29.3)
Atherosclerosis	
Respiratory system	
Asthma	
Chronic obstructive pulmonary disease	8 (19.5)
Allergy	
Metabolic/endocrine	
Diabetes	2 (4.9)

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#### 4. Discussion

The purpose of the present study was to examine the effect of asphalt fume on liver and kidney function tests in road paving workers. Our results demonstrated that liver and kidney function test parameters were significantly higher in the asphalt-exposed group compared to the control group. Although the mean values for all measured liver function tests parameters, urea, and creatinine were within the acceptable reference ranges, there was a significant increase in the serum levels of all parameters suggesting the toxicity of asphalt and bitumen vapors on hepatic and renal tissues. Various kinds of pollutants with different chemical structures are introduced into the environment from industrial activities worldwide [18]. Occupational exposure to asphalt fumes has been of interest because road asphalt paving workers could receive high amounts of hazardous substances such as PAHs and heavy metals by inhalation, dermal contact, and also contaminated food in their workplace. Previous studies on plasma biochemical parameters in road paving workers had shown higher levels of reactive oxygen species, increase DNA damage, and cytogenetic alterations [19, 20]. In the experimental studies, it was concluded that the liver is one of the target organs for toxicity by the bitumen extract [3]. In the initial phase of organ toxicity, the patient looks healthy, and the clinical problem is not apparent [17]. The fact that exposed subjects suffer from

medical complications without exposure to other chemical substances indicates that these problems are likely to be the consequence of exposure to asphalt fumes [17]. More than 63% of study cases had more than 10 years of exposure to asphalt fumes, and all patients with medical complications were among this group. Clinical investigation of cases showed that 22 patients (53.7%) suffered from medical complications attributed to exposure to asphalt fumes.

There is some concern about the safety of nanoparticles and their health risks. Nanoparticles can easily pass through the biological system because of their nanoscale dimensions (smaller than 100 nm) and accumulate in organs up to toxic levels [13, 21]. There is evidence that shows a link between exposure to nanoparticles and respiratory and cardiovascular diseases. Lung deposition and pulmonary toxicity are consequences of nanoparticles with lung tissue. PAHs can cause respiratory problems such as asthma, Chronic Obstructive Pulmonary Disease (COPD), and lung cancer in the exposed workers. PAHs deposit in the alveolar bed through inhalation. Also, PAHs can affect the respiratory system via free radical production after metabolism leading to inflammatory responses and damaging the respiratory system [22].

The toxicity of chemical compounds is estimated biochemically by the tracking of plasma lipids and enzymes

**Table 3.** Length of exposure to asphalt fumes in road asphalt paving workers

Exposure Duration to Asphalt Fumes (y)	No. (%)
5-10	15
11-15	15
15-20	6
> 20	5

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[11]. Chemicals can damage liver tissue in three ways: direct toxicity; production of toxic metabolites resulting from hepatic metabolism; or acting as a hapten, and activation of immune-mediated mechanisms [23]. Several hydrocarbons with aliphatic structures and also PAHs are released during hot application of bitumen and asphalt in road paving process [5, 24]. Carbon-containing compounds and petroleum hydrocarbons are converted to free radicals and other activated metabolites through their oxidation in the liver and kidney cells. Reactive metabolites react with cellular components and produce peroxidation products [5]. Carcinogenicity of bitumen was evaluated by the International Agency for Research on Cancer (IARC) in 2013 [25]. Regulatory agencies such as the Scientific Committee on Occupational Exposure Limits (SCOEL) drew attention to the hazards of bitumen [5]. Integrity and specific functions of hepatocytes can be assessed by monitoring the enzymes as biomarkers [11]. Our results provide further evidence for other studies. Olabemiwo et al. reported elevated ALP activity in rats fed diets containing simulated bitumen leachate [26].

Neghab et al., in their study on road asphalt paving workers, evaluated laboratory results in the exposed and unexposed subjects [17]; however, the present study investigated clinical problems in workers besides laboratory analysis.

One of the findings of the present study is the significant elevation of AST enzyme in the asphalt-exposed group compared to the control group. Just like in our study, previous works confirmed the significant elevation of AST activity in rats exposed to bitumen extract [3]. AST is found in the mitochondria of liver, kidney, and heart cells. Therefore, the increased level of AST can be an indicator of hepatocytes permeability and necrosis. Like our study, Farombi et al. revealed organ toxicity in rats treated with landfill leachate [27]. The other finding of the present study was a significant elevation in plasma triglyceride level in road paving workers compared to the control group. Previous studies confirmed that hepatotoxicity in the experimental rat model could be assessed by plasma triglyceride assay. Otuechere et al. had already reported a similar finding of an increased level of triglyceride in an experimental rat model exposed to bitumen extract [3].

Contrary to our findings, decreased levels of AST and ALT were reported for those subjects occupationally exposed to petroleum oil [28]. According to previous reports, certain environmental agents such as aromatic hydrocarbons can cause enzyme induction and, conse-

quently, elevation in AST, ALT, and ALP activities [28]. Elevated serum level of bilirubin was recorded in experimental models study. When bile secretion from hepatocytes to the canaliculi is impaired, the flow of bile through the biliary tract is obstructed. In this condition, the plasma bilirubin level is increased [28]. Chronic exposure to toxic elements such as Cr, Cd, Pb, and Ni results in accumulating the element in the liver and kidney tissues, causing organ malfunctioning [29]. Asphalt and bitumen contain heavy metals such as Cd, Pb, and Mn [30]. Markiewicz-Górka et al. in their study on chronic combined exposure to low environmental doses of Cd, Pb, and Mn found that elevated serum bilirubin level is known as a result of liver and biliary tract dysfunction and toxic changes in the liver were correlated with high concentrations of Cd, Pb, and Mn in blood [31].

In contrast to the present study results, Bommarito et al. showed reduced activities of ALT and AST in newts exposed to coal-tar and asphalt sealants. They concluded that PAHs are lethal and sublethal compounds. However, ultraviolet radiation and oxidation of PAHs generate some degradation products that are more toxic than the parent compound [32].

According to the results of the present study, the mean serum creatinine level was significantly higher in the asphalt-exposed group compared to their non-exposed counterparts. Kidney dysfunction can be manifested by microscopic hematuria and abnormal serum creatinine and urea levels [33]. Also, Abusoglu et al. stated that urinary total oxidant status levels were higher for asphalt workers compared with other occupational groups [34]. However, Awasthi et al. reported that exposure to petroleum fumes for a maximum of five years did not affect serum creatinine level [11].

## 5. Conclusion

The present study signified that although the level of assayed hepatic and renal biochemical markers was within the parameters reference ranges in road asphalt paving workers, a significant increase in biochemical markers suggested that asphalt and bitumen vapors produce some hepatotoxic and nephrotoxic substances. Periodic medical examination, protective equipment, and personal cleanliness can minimize the risk of organ toxicity among road asphalt paving workers.

## Study Limitations

Our study should be interpreted within the context of its possible limitations. First, we have no information



about the composition of asphalt used. Second, we could not estimate heavy metals, PAHs, and their metabolites in the urine or plasma samples. However, these limitations did not overshadow the main purpose and obtained results of the present study.

Further studies are needed to assess the health effects of bitumen fumes on asphalt workers at the cellular and molecular level to estimate oxidative damage to liver and kidney tissues.

## Ethical Considerations

### Compliance with ethical guidelines

The study procedures were conducted following the Helsinki Declaration and its later amendments. All study samples information was kept confidential, and the study was approved by the Ethics Committee of Legal Medicine Research Center, Legal Medicine Organization, Tehran, Iran.

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### Author's contributions

All authors equally contributed to the design, sample collection, laboratory analysis, and writing of all research parts.

### Conflict of interest

The authors reported no potential conflict of interest.

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