The Effect of Benzene Exposure on Liver and kidney Function in Human

Abstract:

Background: Exposure to benzene in the workplace causes health issues for the workers, it has negative impacts on the blood, liver, and kidney. Also, it is classified as carcinogenic.

Methods: This study is cross-sectional; it involved 32 participants; 16 exposed to benzene and 16 non-exposed. The sample was collected by filling out a questionnaire and taking blood samples to test liver and kidney functions.

Result: This study found that the means of AST and ALT levels of exposed workers were lower than the control group, while the mean level of ALP was higher. Moreover, it did not find a relationship between qualification, years of experience, age, and level of liver enzymes of exposed participants, however, it reported a positive correlation between smoking and bilirubin level.On the other hand, there are no statistical differences between the two groups in the levels of urea and creatinine, but the mean of urea level was quite higher in the exposed group than non-exposed. Besides, there are no associations between urea and creatinine levels and age, qualification, smoking, and years of experience.

Conclusion: This study demonstrated a clear association between exposure to benzene and its effect on the liver. Therefore, suitable precautions should be taken to protect the workers in the gas station.

Key Words: ALP, ALT, AST, Benzene, Creatinine, Exposure, Liver and Kidney Functions, Urea.

Introduction:

Benzene is a colorless liquid that is commonly used in industry [1]. It is classified as carcinogenic [2], and it has negative impacts on the workers' health, it affects on the eyes, skin, airway, nervous system, and lungs [3]. Also, it can cause changes in blood counts [4], and blood cancers like leukemia [3]. Its toxicity is the most commonly caused by the inhalation of benzene in the surrounding air [5, 6].

Benzene is absorbed in the body after inhalation or oral exposure in the workplace. Then, it transfers to the blood through passive diffusion [7]. After that, the absorbedbenzene is distributed everywhere in the body [8], and it is metabolized into a number of reactive types such as phenol, catechol, and hydroquinone [9].

The first step of benzene metabolism is oxidation to the reactive intermediate benzene oxide by the cytochrome P450 enzyme in ltheiver. Benzene oxide can undergo several phases; it could undergo to non-enzymatic rearrangement to form phenol. On the other hand, it could hydrolyze via epoxide hydrolase to a dihydrodiol, also, its ring can open to form trans, trans- muconaldehide (ttMA) via the reactive intermediate muconaldehyde, or conjugate with glutathione to ultimately. Phenol and the dihydrodiols can undergo further metabolism to produce hydroquinone or catechol. The metabolite profile in the liver appears to be similar to that found in the kidney, except that the relative percentages of muconic acid and unconjugated phenol were lower in the liver than in the kidney. The second step includes the oxidation of hydroquinone to benzoquinones, and that could turn back to hydroquinine or catechol by NAD(P)H dehydrogenase [quinone] 1 enzyme. Benzoquinones are generally considered to have the highest toxicity, and phenolic conjugates are formed in the liver and it transfered via the blood to the bone marrow, where they are hydrolyzed and oxidized to quinones[10].
The main way for benzene elimination is exhaled via the lungs, and its excretion rate are depending on the dose and route of exposure [11]; stable metabolites are secreted in urine (mainly phenol), therefore, the phenolic compounds (phenol, catechol, and hydroquinone) are detected in human urine [12]. These metabolites play a major role in benzene toxicity, causing cytogenetic modifications and chromosomal aberrations [13,14, 15].

Moreover, benzene leads to an increase in the liver enzymes (aspartate aminotransferase AST, alkaline phosphatase ALP, and alanine aminotransferase ALT), and total changes in bilirubin and fatty liver, and it could lead to neural and liver damage and kidney cancer [16].
Reviewing past literature, exposure to benzene leads to a reduction in the levels of ALP, ALT, and albumin and an elevation in the levels of total protein in people who are exposed to benzene [17].
On the other hand, other previous studies observed that benzene exposure leads to increases in the levels of ALP, AST, and ALT of exposed participants [16, 18, 19, 20, 21], an increase in the level of creatinine [22], and an increase in the urea level of exposed groups [16,21, 23].

Aim:To determine whether benzene has an effect on liver and kidney functions in exposed workers at OiLibya420 Gas Station, Benghazi, Libya.

Material and methods:

Study site: This study was carried out at the OiLibya420 Gas Station in Benghazi, Libya.

Study design:it is a cross-sectional design. It was conducted from July to August 2020.

Method of data collection: The data was gathered in two ways: the first way was using a multiple-choice questionnaire that contains questions regarding age, years of experience, and level of education. And the second way was by taking blood samples to test renal and liver functions

Target population and sample size

The samples included 32 participants; 16 exposed workers to benzene in filling station and 16 non-exposed participants.

Statistical analysis

All date were coded and analyzed using SPSS version 22. The frequency and percentage of some variables were calculated. Additionally, to identify the relationship between variables, this study uses Mann-Whitney and Kruskal-Wallis tests.

Limitation

The limitations of this study included a small sample size; which wAS 16 exposed participants working in this petrol station. This station is the biggest station in Benghazi, therefore, this study involved all the workers in this station.

Results and findings

The sample involved 32 participants: 16 exposed to benzene in the OiLibya420 Gas Station and 16 non-exposed to benzene.

Table 1 shows that 9 out of 16 exposed workers had less than 5 years of experience, while 4 workers had experience between 16 to 20 years. Moreover, 8 workers had a preparatory qualification level, 4 had a diploma, 3 had a high school level, and only 1 had a bachelor's qualification level. Besides, the table shows that a high percentage of participants are currently smokers (56.3%), 6.3% was previously smokers, and 37.5% were never smokers.

Table 1: Characteristics of workers exposed to benzene in OiLibya420 Gas Station

Characteristics		No. (%) Exposed group
Years of experience	0-5	(56.3%) 9
	6-10	(6.3%) 1
	11-15	(0%) 0
	16-20	(25%) 4
	21-25	(0%) 0

	More than 26	(12.5%) 2
Qualification level	Preparatory	(50%) 8
	High school	(18.8%) 3
	Diploma	(6.3%) 4
	BSc	(25%) 1
Smoker	Never	(37.5%) 6
	Current smokers	(56.3%) 9
	Pervious smoker	(6.3%)1

Liver Function Test (LFT):

Table 2 shows normal levels of AST for the non-exposed group. However, the mean of AST levels was low for the group of cases compared to the normal range of AST in the human body (Figure 1).

Table 2: AST levels of exposed and non-exposed groups

AST levels	Exposed group	Non-exposed group
Below normal level	1	0
Normal level	15	16
Above normal level	0	0
Mean level of AST	13.8	17.1

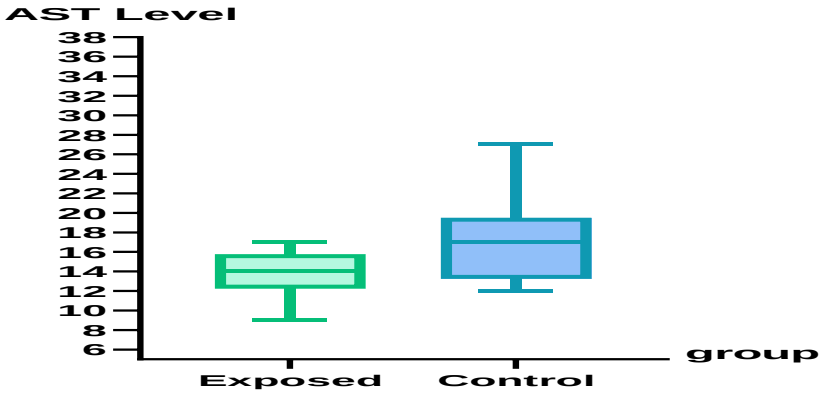

Figure 1: Means of AST enzyme levels in exposed and non-exposed groups

Additionally, Table 3 shows acceptable levels of ALT in both groups compared to the normal level of ALT, however, it observed a slightly deficient level in the exposed group compared to the non-exposed group, indicating that mean ALT of the exposed group was lower than the mean of the non-exposed group, which was 14 and 20.3 respectively (Figure 2).

Table 3: ALT levels of exposed and non-exposed groups

ALT levels	Exposed group	Non-exposed group
Below normal level	1	0
Normal level	15	16
Above normal level	0	0
Mean level of ALT	14	20.3

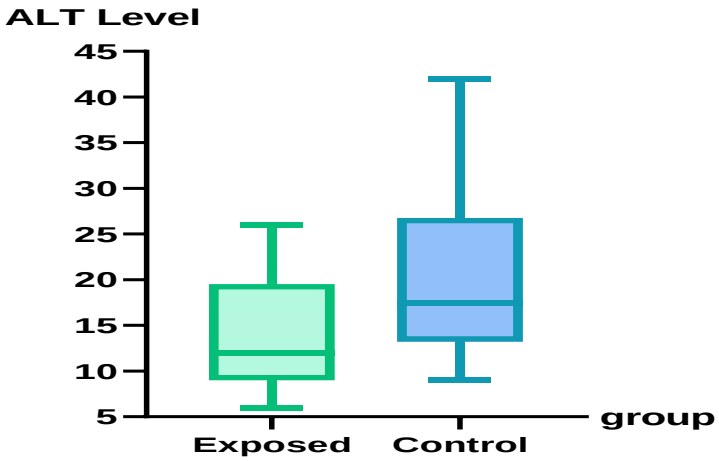

Figure 2: ALT enzyme level of exposed and non exposed groups

Also, the next table (4) represents the normal levels for the most participants in both groups, and the most tendencies to the upper limit of the normal level were observed in exposed workers (Figure 3).

Table 4: ALP levels of exposed and non-exposed groups

ALP levels	Exposed group	Non-exposed group
Below normal level	0	0
Normal level	14	16
Above normal level	2	0
Mean level of ALP	99.2	79.6

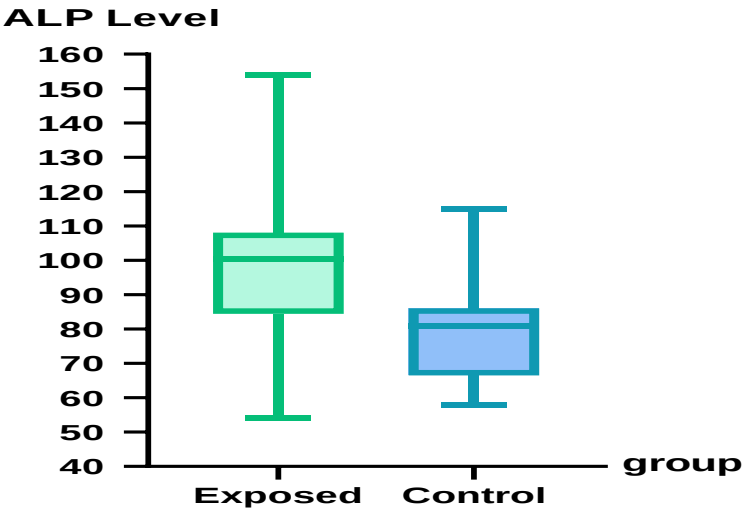

Figure 3: ALP enzyme level of exposed and non exposed groups

Table 5 shows that bilirubin levels for both groups were approximately normal, and it shows the means of bilirubin between the two groups are quite similar (Figure 4).

Table 5: Bilirubin levels of exposed and non-exposed groups

Bilirubin levels	Exposed group	Non-exposed group
Below normal level	0	0
Normal level	15	16
Above normal level	1	0
Mean level of Bilirubin	0.59	0.51

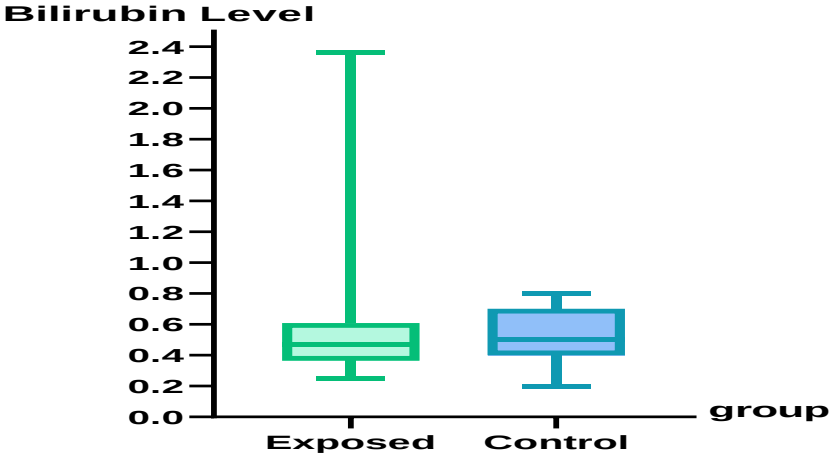

Figure 4: Bilirubin level of exposed and non exposed groups

Table 6 indicates that there are statistical differences in the levels of liver enzymes (ALT, AST,and ALP) between exposed and non-exposed, and a lack of relationship to the level of bilirubin between the two groups.

Table 6: Association between liver function tests and exposed and non exposed groups using the Mann-Whitney Test

Liver Function Test	Mann-Whitney	Wilcoxon W	Z	Asymp. Sig.
AST	67.500	203.500	-2.295	0.022
ALT	74.000	210.000	-2.039	0.041
ALP	61.500	197.500	-2.510	0.012
Bilirubin total	114.000	250.000	-0.530	0.596

Furthermore, Table 7 shows the absence of a relationship between the qualification and the level of enzymes (AST, ALT, and ALP) in exposed and non-exposed groups. Also, there is no correlation between the qualifications of both groups and their bilirubin levels.

Table 7: Association between liver function tests and qualification levels using the Kruskal-Wallis Test.

Liver Function Test	Chi-Square	df.	Asymp. Sig.
AST	2.568	3	0.463
ALT	4.658	3	0.199
ALP	1.748	3	0.626
Bilirubin total	1.460	3	0.692

Besides, Table 8 shows that there is no relationship between years of experience of workers and the level of liver enzymes (ALT, AST, and ALP) and bilirubin, depending on the p-value.

Table 8: Association between liver function tests and years of experience using the Kruskal-Wallis test.

Liver Function Test	Chi-Square	df.	Asymp. Sig.

AST	5.601	3	0.133
ALT	4.456	3	0.216
ALP	0.964	3	0.810
Bilirubin Total	5.615	3	0.132

Table 9 shows that workers' age is not correlated with levels of liver enzymes (ALP, ALT, and AST) or bilirubin levels, depending on the significant p value.

Table 9: Association between liver function tests and workers ages using the Kruskal-Wallis test.

Liver Function Test	Chi-Square	df.	Asymp. Sig.
AST	5.672	3	0.129
ALT	1.698	3	0.637
ALP	0.145	3	0.986
Bilirubin Total	4.022	3	0.259

Table 10 shows no relationship between smoking and levels of liver enzymes (ALP, ALT, and AST), while there is a relationship between the level of bilirubin and smoking, depending on the significant p value.

Table 10: Association between liver function tests and smoking using the Kruskal-Wallis test.

Liver Function Test	Chi-Square	df.	Asymp. Sig.
AST	2.402	2	0.301
ALT	2.166	2	0.339
ALP	0.225	2	0.894
Bilirubin Total	6.228	2	0.044

3.4 Renal Function Test (RFT):

Regarding the RFT, table 11 shows normal urea levels for both groups, with a tendency to be higher in the exposed group (Figure 5).

Table 11: Urea levels of the exposed and non-exposed groups

Urea levels	Exposed group	Non-exposed group
Below normal level	0	0
Normal level	15	15
Above normal level	1	1
Mean level of Urea	29.6	27.6

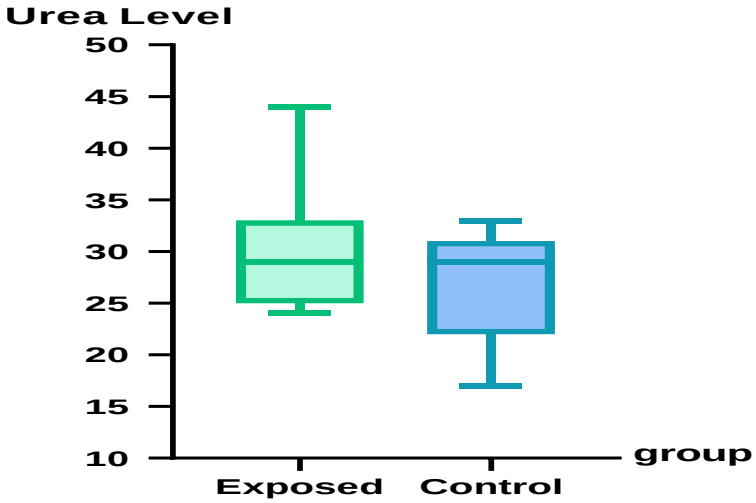

Figure 5: Urea level of the exposed and non exposed groups

Regarding Table 12, it represents the level of creatinine in two groups as normal.It shows that the exposed participants have a lower mean than the non-exposed participants (Figure 5).

Table 12: Creatinine levels of the exposed and non-exposed groups

Creatinine levels	Exposed group	Non-exposed group
Below normal level	0	0
Normal level	16	16
Above normal level	0	0
Mean level of Creatinine	0.86	0.89

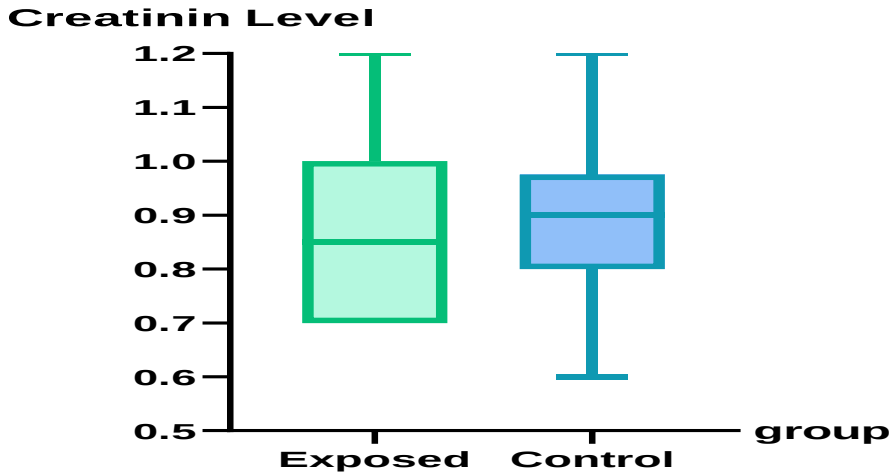

Figure 6: Creatinine Level of exposed and non-exposed groups

Table 13 shows there is no statistical relationship between urea and creatinine levels among exposed and non exposed groups because p values were greater than 0.05.

Table 13: Association between renal function tests and exposed and non exposed groups using the Mann-Whitney test

Renal Function Test	Mann-Whitney U	Wilcoxon W	Z	Asymp. Sig.
Urea	107.000	243.000	-0.795	0.427
Creatinine	112.000	248.000	-0.616	0.538

Besides, Table 14 reported that there is no relationship between qualification level and urea and creatinine levels of the exposed participants because p values are greater than 0.05.

Table 14: Association between renal function tests and Qualification using the Kruskal-Wallis Test

Renal Function Test	Chi-Square	Df	Asymp. Sig.
Urea	5.299	3	0.151
Creatinine	4.986	3	0.173

Additionally, Table 15 shows that there is no statistical relationship between the experience years of exposed workers and urea and creatinine levels because p values were greater than 0.05.

Table 15: Association between renal function tests and years of experience using the Kruskal-Wallis Test

Renal Function Test	Chi-Square	df.	Asymp. Sig.
Urea	4.290	3	0.232
Creatinine	5.913	3	0.116

Furthermore, Table 16 reported that there is a statistical relationship between age and Urea levels of exposed workers because the p value is less than 0.05. While there is no relationship between age and creatinine levels of exposed workers because p value was greater than 0.05.

Table 16: Association between renal function tests and workers' age using the Kruskal-Wallis test

Renal Function Test	Chi-Square	df.	Asymp. Sig.
Urea	8.847	3	0.031
Creatinine	2.037	3	0.565

Furthermore, Table 17 shows there is no statistical relationship between smoking and the urea and creatinine levels of exposed workers because the p values are greater than 0.05.

Table 17: Association between renal function tests and smoking using the the Kruskal-Wallis test

Renal Function Test	Chi-Square	df.	Asymp. Sig.
Urea	0.419	2	0.811
Creatinine	0.678	2	0.713

Discussion:

The effects of benzene exposure on liver function Tests:

The present study found that most of the enzymes responsible for liver function in both groups were at an acceptable level for most participants compared to the normal range in the body, with more tendencies to decrease in some enzymes among exposed participants. Also, it was reported that there is a statistical difference in ALT, AST, and ALP between exposed and non-exposed workers.Similarly, Akinosun et al. (2006) reported that ALP was lower in exposed individuals than non exposed workers in Nigeria, and other parameters such as AST, ALT, and total bilirubin were similar in both groups [24]. Additionally, Nwanjo and Ojiako found a significant increase in the activities of ALP, ALT, and AST in the workers in twenty petrol station attendants in Owerri, Imo State, Nigeria, while there was no significant change in the plasma bilirubin concentrations between exposed and non exposed groups [25].

Furthermore, the present study indicated no relationship between liver function and the age of workers. In contrast, Neghab et al. (2015) found a positive relationship between age and levels of AST and ALT, but they did not find correlation between age and levels ALP and bilirubin [16].

Moreover, the present study indicated that there was no relationship between the workers' years of experience and the level of enzymes responsible for liver function. This is contrast to the study conducted by Nwanjo and Ojiako indicated that levels of AL, ALT and AST were higher among exposed workers who had years of experience ranging from 6 to 10 years [25].

Besides, the current study indicated that the level of enzymes responsible for liver function did not correlate with the educational qualifications of workers. On the other hand, no study has discussed the relationship between worker qualification and liver function tests.

Regarding smoking, this study indicated that there was no relationship between the level of liver enzymes (ALT, AST, and ALP) and smoking, while there was a correlation between the level of bilirubin and smoking. And this comes in disagreement with the study carried out by Neghab et al. which found a positive relationship between smoking and the levels of AST and ALT and no correlation between smoking and the levels of ALP and bilirubin [16].

The effects of benzene exposure on renal function Test:

The present study reported that exposure to benzene could lead to elevated the urea levels, while no clear effect was found on creatinine. In line with previous studies, Bin-Mefrij&Alwake indicated that exposure to benzene causes an increase in the levels of serum creatinine and urea [23].Besides, Neghab et al. found an elevation in the levels

of blood urea and creatinine in exposed participants more than in non-exposed participants [16].Moreover, Mark & Reddy indicated a remarkable increase in the levels of creatinine in the exposed benzene group compared to the non-exposed group [20].

Furthermore, the current study found a statistical relationship between age and urea levels of exposed workers, while there is no relationship between age and creatinine levels of exposed workers. In contrast, El-awad et al. reported no significant difference between renal function tests and worker age [22].

Additionally, this study reported no statistical relationship between the experience years of exposed workers and urea and creatinine levels. In comparison with prior studies, Nwanjo&Ojiako observed an elevation in the concentration levels of urea and creatinine among groups exposed to fuel vapor for 6 to 10 years compared to the control group [25], and this is consistent with previous results of another study that found that serum urea and mean serum creatinine concentration levels were higher among study participants who were exposed to gasoline and diesel fumes for more than 5 years [23].
Also,the current study found no relationship between the qualification level of exposed workers and urea and creatinine levels. On the other hand, no study has tested this type of relationship before now.

Moreover, the present study indicated no statistical relationship between smoking and urea and creatinine levels among exposed workers, Moreover, there is no research testing the association between smoking and the effects of benzene on renal.

Conclusion:

This paper has highlighted the relationship between exposure to benzene and its effect on liver and renal functions. It found a clear difference in the level of liver enzymes (ALT, AST, and ALP) between the two groups. Besides, it did not find any relationship between age, years of experience, or qualification level with liver function. While it concluded a positive relationship between the effects of benzene on bilirubin levels and smoking, additionally, it found no a relationship between the effects of benzene on RFT and workers' qualification level, experience years and smoking. However, it found an obvious correlation between age and the effects of benzene on the urea levels of exposed workers, while it found a negative relationship between age and creatinine levels.

Ethical Approval:

This study began after sending a preliminary letter to the manager of the OiLibya420 Gas Station and getting permission to take blood samples to do liver and renal function tests.

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