

# **HEPATITIS FOLLOW UP AMONG PESTICIDE FORMULATORS**

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## **ABSTRACT**

The liver is the target organ of many occupational and environmental agents and plays a central role in their detoxification as well as the elimination of many toxic chemicals and/or their metabolites .

A previous study was done three years ago on 389 subjects in a chemical factory for pesticide formulators, it revealed that there was a significant seroprevalence of HCV & HBV among studied workers as well as significant elevation of ALT enzymes among both seropositive and seronegative HCV & HBV .

This work was done on 150 selected workers from a previous study three years ago in a chemical factory formulating pesticides. All selected subjects were assessed by clinical examination regarding complications and risk factors of hepatitis, laboratory investigations and abdominal ultrasonography.

We concluded from this study that there is an increase in the curve of progression of chronic liver disease among studied subjects on follow up and this may be due to presence of another contributing factor which is chronic exposure to pesticides.

## Introduction

Hepatitis B and C are common infections worldwide and may give rise to hepatic cellular carcinoma, which is one of the most common cancers, and progresses to cirrhosis even after a long symptomless course (Akimkin et al., 1997).

Although the prevalence of HCV infection in Egypt is high, yet little is known about the risk factors, the pathogenicity and the virology features of HCV ( Angeli-co et al., 1997) .

Humans are exposed to pesticides in a variety of occupational settings including agriculture, structural pest control, public health pest eradication programs, formulators' transportation industries (Sckenker et al., 1998).

The severity of any adverse effect from exposure to pesticides depends on the dose, the route of exposure, absorption of pesticides, the type of the pesticide, its metabolites, its accumulation and persistence in the body. The toxic effects also depend on the health status of the individual. Malnutrition and dehydration are likely to increase sensitivity to pesticides (WHO, 1990).

Pesticides exposure may play a greater role in suspected fragile immune system, and may result in altered disease suscepti-

bility. Immune dysfunction is related to dose and duration of pesticide exposure (Banerjee et al ., 1996) .

## Materials and Methods

### Sample selection

Our sample was selected as follows: 150 workers were randomly selected from 270 workers who have already been included in a previous study. A numbered list of those 270 workers was obtained from the investigator, and using EPIINFO software ver.6, 150 random numbers were generated from 1 - 270. The generated numbers designated the workers to be included in our study.

All selected subjects were assessed by : full history taking and clinical examination including risk factor of hepatitis and its complications, laboratory investigation as ALT , abdominal ultrasonography was also assessed and the impact of treatment in the form of liver support on subgroup and whether this treatment affects the clinical , laboratory and ultrasound findings or not.

Abdominal ultrasonography: was done for the available subjects using an ultrasound machine (Hitachi, EUB200) with a 3.5MZ linear transducer.

## Statistical analysis

Statistical analysis were performed: the mean value or the average, Standard deviation, Paired t test and McNemar test.

The computer software SPSS version 9 was used to get the significance from appropriate applied tests.

## Results

The group of this study was composed of 150 male workers with mean age of (45.26 ±6.9) ranging from (27-59 years) & duration of exposure of (20.57 ±6.15) with a range of (7-35 years) .

The frequency of different pesticides exposure during production was as follows: organophosphate 55 (36.7%), organochlorine 23 (15.3%), pyrethroids 56 (37.3%), Zn phosphide 16 (10.7%).

The seroprevalence of hepatitis among studied subjects (from the previous assessment) was: HBV seropositive only (30%), HCV seropositive only (12%), and HCV & HBV seropositive (39.3%).

Thirty one of the studied subjects were receiving drugs in the form of liver support and DDB (dimethyl dimethoxy bi-phenyl dicarboxylate ) for one year duration .

Table (1) presents risk factors of hepatitis among the studied subjects .The num-

ber of subjects with history of exposure to hazards of surgical intervention significantly increased on follow up ( $p < 0.01$ ) . On the other hand, there is no statistically significant difference in other risk factors between the 1st assessment and follow up ( $p > 0.05$ ) .

Table (2) presents the clinical features among the studied subjects showed that cases with enlarged spleen as well as cases with shrunken liver significantly increased on follow up  $p < 0.05$  .

Table (3) presents echo assessment among the studied subjects which demonstrated a statistically significant increase in the frequency of cirrhosis , splenomegaly and ascitis among the studied subjects on follow up ( $P < 0.05$ ) while the frequency of hepatomegaly significantly decreased on the follow up ( $P < 0.05$ )

Table (4) presents the mean ALT of the studied subjects significantly increased during follow up Paired t = -3.199 ,  $P = 0.002$

The mean ALT level in subjects receiving treatment decreased on follow up yet , this change was not statistically significant ( $p < 0.05$ ) on the other hand, the mean ALT level in subjects not receiving any treatment significantly increased on follow up ( $P < 0.001$ ) fig(1) .

Table (5) presents The mean ALT level in HB &HC positive subjects receiving treatment decreased on follow up yet, this change was not statistically significant  $P>0.05$  on the other hand the mean ALT level in similar subjects not receiving any treatment significantly increased on follow up  $P<0.001$ .

Table (6) presents the changes in the frequency of the different clinical findings during follow up showed no statistically

significantly different from 1st assessment in both treated and untreated cases with both hepatitis B and hepatitis C . As regards the echo assessment table (7) showed the frequency of cirrhosis, and ascites significantly increased among subjects with positive hepatitis B and C not receiving any treatment, on the other hand the increase in the frequency of these findings among subjects receiving treatment was not statistically significant

Table(1) : Risk factors of hepatitis among the studied subjects

	History				P value
	1 <sup>st</sup> assessment		Follow-up		
	Frequency	Percent	Frequency	Percent	
Smoking	71	47.3%	72	48%	>0.05
Bilharzial treatment	88	58.7%	88	58.7%	>0.05
History of hepatitis	25	16.7%	26	17.3%	>0.05
Blood transfusion	13	8.7%	15	10%	>0.05
Dental treatment	138	92%	138	92%	>0.05
Parenteral treatment	146	97.3%	146	97.3%	>0.05
Surgery	77	51.3%	98	65.3%	<0.01

Table (2) : Clinical features among the studied subjects .

	Clinical examination				P value
	1 <sup>st</sup> assessment		Follow-up		
	Frequency	Percent	Frequency	Percent	
Vitamin deficiency	77	51.3%	77	51.3%	>0.05
Jaundice	9	6%	10	6.7%	>0.05
Splenomegaly	37	24.7%	44	29.3%	<0.05
Hepatomegaly	45	30%	39	26%	>0.05
Shrunken liver	11	7.3%	19	12.7%	<0.05

Table (3) : Echo assessment among the studied subjects .

	Ultrasonographic findings				P value
	1 <sup>st</sup> assessment		Follow-up		
	Frequency	Percent	Frequency	Percent	
Fibrosis	49	32.7%	51	34%	>0.05
Cirrhosis	25	16.7%	41	27.3%	<0.01
Hepatomegaly	77	51.3%	66	44%	<0.05
Splenomegaly	82	54.7%	96	64%	<0.01
Ascites	2	1.3%	13	8.7%	<0.05

Table (4) : ALT level among the studied subjects .

	Mean	SD
ALT 1st assessment	29.24	14.98
ALT follow up	34.51	18.64

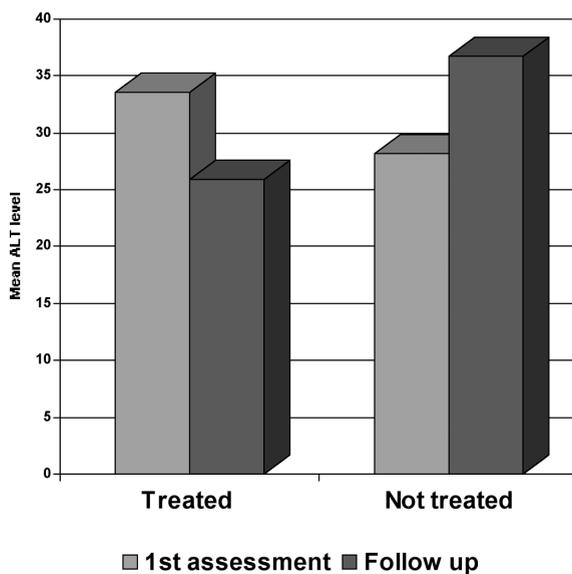


Figure (1) : ALT changes in treated and untreated subjects.

Table (5) : ALT changes in treated and untreated subjects in seropositive HBV & HCV subjects .

	Treated cases		Untreated cases	
	Mean ALT	SD	Mean ALT	SD
1st assessment	33.56	17.4	27.21	12.15
Follow-up	25.56	13.59	40.25	19.74
Paired t-test	1.266		-4.161	
P value	>0.05		<0.001	

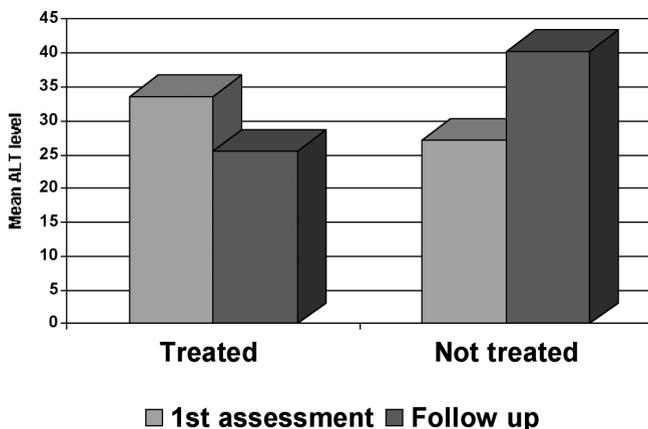


Figure (2) : ALT changes in treated & untreated seropositive HBV & HCV subjects .

Table (6) : clinical findings among treated and untreated subjects .

		Clinical examination				P value
		1st assessment		Follow-up		
		Frequency	Percent	Frequency	Percent	
Vit . def.	Treated	21	67.7%	21	67.7%	>0.05 (NS)
	Untreated	56	47.1%	56	47.1%	>0.05 (NS)
Jaundice	Treated	3	9.7%	2	6.5%	>0.05 (NS)
	Untreated	7	5.9%	7	5.9%	>0.05 (NS)
Hepatomegaly	Treated	9	29%	8	25.8%	>0.05 (NS)
	Untreated	36	30.3%	31	26.1%	>0.05 (NS)
Shrunken Liver	Treated	3	9.7%	5	16.1%	>0.05 (NS)
	Untreated	8	6.7%	14	11.8%	0.031
Splenomegaly	Treated	7	22.6%	9	29%	>0.05 (NS)
	Untreated	30	25.2	35	29.4%	>0.05 (NS)

Table (7) : Echo assessment among treated and untreated subjects.

		Ultrasonographic findings				P value
		1st assessment		Follow-up		
		Frequency	Percent	Frequency	Percent	
Fibrosis	Treated	11	35.5%	11	35.5%	>0.05 (NS)
	Untreated	38	31.9%	40	33.6%	>0.05 (NS)
cirrhosis	Treated	6	19.4%	9	29%	>0.05 (NS)
	Untreated	19	16%	32	26.9%	<0.001
Hepatomegaly	Treated	18	58.1%	14	45.2%	>0.05 (NS)
	Untreated	59	49.6%	52	43.7%	0.016
Splenomegaly	Treated	18	58.1%	22	71%	>0.05 (NS)
	Untreated	64	53.8%	74	62.2%	0.002
Ascites	Treated	0	0%	3	9.7%	>0.05 (NS)
	Untreated	1	0.8%	10	8.4%	0.004

## Discussion

As regards the history this study showed that no statistically significant difference in the risk factors as smoking , bilharzial treatment , blood transfusion , dental or parenteral treatment between the 1st assessment and follow up, but there was a significant difference in surgical procedures between the 1st assessment (51%) and follow up (65.3%) . These results agreed with Edward et al., 2000 who studied the risk factors of hepatitis C virus infection of 758 seropositive blood donors in the Untied States , deduced that 74% had history of surgery and 77% had sutures .These results also agreed with Zeurem et al., 1996 who suggested that up to 40 % of HCV seropositives do not recognize parenteral risk factors , leading to the speculation that other , yet undiscovered modes of transmission may exist .

According to Hayes (1991) pesticides could induce fatty changes in the liver , due to a number of factors e.g. organelle injury , metabolic disorder , deficiency of essential lipophilic sources , or varying combinations of any of these factors .

Our findings were not concomitant with Amr et al., 1994 in his survey study on 242 male applicators in which 18% , 32% had hepatomegaly and splenomegaly, respectively . And this may be due to the

possibility of increased incidence of bilharzial infestation in the group of applicators , while our studied group were chronically exposed to pesticides .

As viral hepatitis competes with schistosomiasis as a leading cause of chronic liver diseases in Egypt ,this can explain why our studied group showed high frequency of HCV 77(51%) seropositive as well as exposure to different types of pesticides in addition that 88(58.7%) of them received anti-bilharzial treatment which is one of the contributing factor of this higher results

In 1991, Hayes claimed that by ultrasound , fatty liver (bright echogenicity) , cirrhosis (coarse echogenicity) and possibly chronic hepatitis accompanied by increased fibrous tissue, the diagnosis could be made easily, while it was uncertain in mild chronic active and chronic persistent hepatitis .

In our study, abdominal ultrasonography showed that there was a statistically significant increase in the frequency of cirrhosis (16.7%) , splenomegaly (54.7%) and ascites (1.3%) between the 1st assessment and the follow up group (27.3%) , (64%) & (8.7%) respectively . These results were concomitant with Amr et al., 1994 who showed that most of the applicators (n=242) with triple insults (pesticides

exposure schistosomiasis and or viral hepatitis) had liver abnormalities (90%) while about (53%) of applicators of the second group (pesticides only) had liver abnormalities by ultrasonography.

This agreed with El-Gazzar et al., 1989 and Amr et al., 1990 in their studies conducted on pesticides formulators, which confirmed the possible interaction or synergism between the biological (schistosomiasis and or viral hepatitis) and chemical (pesticides) insults on liver .

The mean ALT of the studied workers show significant increase during follow up . These results are concomitant with Kamal et al., (1990), in his study on pesticides sprayers in Egypt, who suggested that these findings may be due to the phenomenon of enzyme induction and he added that this also might indicate that this parameter may reflect the hepatic affection of long term exposure to pesticides .

Our results also agreed with Kossmann et al., (1997) who assessed the liver damage in workers employed at the production of chlorfenvirphos (organophosphates) .

Gao et al., (1998) explained the efficiency and safety of DDB (Dimethyl Dimethoxyl Biphenyl Dicarboxylate ) in treatment of severe chronic hepatitis C, possibly through immunomodulator ef-

fects which protect the hepatocytes against invasion and necrosis by HCV, via stabilization of cell membrane of hepatocytes or both actions .

Thirty one of our workers in this study received treatment in the form of nonspecific drugs (liver support) and DDB for one year duration .We found that the mean ALT level in patients receiving treatment decreased on follow up , yet this change was not statistically significant. On the other hand, the mean ALT level in subjects not receiving treatment showed statistically significant increase on follow up.

As regards clinical examination, the frequency of shrunken liver showed statistically significant increase on follow up among subjects not receiving treatment , while the increase in frequency of shrunken liver among subjects receiving treatment was not statistically significant.

Montasser et al., (1999) in his study on DDB for treatment of 25 chronic HCV patients , concluded that DDB was beneficial for treatment of chronic HCV patients as it improved the clinical symptoms and induced sustained normalization of serum ALT with statistically significant drop in serum ALT without undesirable effects. When comparing the clinical , biochemical and hematological results in patients treated with DDB only with patients

treated by DDB and silymarin , there was no statistically significant difference. When he compared the clinical and biochemical results in patients with no HSM with those who had HSM he found clinical improvement more evident in those patients with no organomegaly .

In our study the statistically non significant decrease in mean ALT level in patients receiving treatment may be due to another contributing factor which is long duration of exposure to pesticides during formulation

This could be due to pesticides intoxication which suppresses the mediated immunity of the subjects , so they will be more prone to get HCV and other viruses than the general population .

From this study we can conclude that HCV is a chronic disease and its curve of progression is going upward on follow up , in addition to pesticides exposure which has a definite hepatotoxic effect. HCV is a chronic disease it may lead to disability of the workers through its complications as liver cell failure , esophageal varices leading to haematemesis , lastly hepatocellular carcinoma (HCC) and death . Although non of our studied subjects showed HCC , yet there was statistically significant increase in liver cirrhosis and ascites by abdominal ultrasound assessment .

We need further investigations as upper GI endoscopy and liver biopsy to follow the rate of complications in the studied subjects and PCR to follow up the level of viraemia of those who are HCV +ve . We also need to compare this follow up with that in the general population to find out if there is a significant difference or not .

Pre-employment study of the immune system and screening for HCV together with follow up of those who are HCV -ve workers after a period of exposure to pesticides during formulation will detect whether pesticides decrease the immune system and cause the worker to be more prone to viral infections as HCV or there are other risk factors that contribute to the increased incidence of infection in this group .

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