

# OZONE THERAPY IN PATIENTS WITH VIRAL HEPATITIS “C” TEN YEARS EXPERIENCE

By

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# Why HCV?

- Worldwide medical problem (estimated that more than 300 millions suffering from HCV)
- Major medical problem in EGYPT (postulated that more than 15% i.e. more than 10 millions of the population are suffering from HCV)
- Slowly progressing, detected mainly accidentally, devitalizing and difficult to treat

# Why HCV? (cont.)

- In most cases it leads to complications e.g. liver cirrhosis, ascitis, liver carcinoma and ultimately liver cell failure
- Not only a medical problem, but also an economic problem (less work, less production and very high costs of usual treatment)

# Immune Activating effect of Ozone

- Many researches has proved that ozonized blood releases interferons (IFN- $\alpha$ , IFN- $\beta$ , and IFN- $\gamma$ ), Interleukins (interleukins of the types IL-1b, 2, 4, 6, 8, 10), tumor necrosis factor (TNF -  $\alpha$ ), granulocyte macrophage colony-stimulating factor (GM-CSF) and the transforming growth factor TGF- $\beta$ 1. (Bocci et al 1990 & 1993, Paulesu et al 1991, Larini et al 2001)

# Immune Activating effect of Ozone (cont.)

- Interferons with their antiviral activity prevent viral replication, additionally activating basic immunomodulatory functions together with interleukin-2 and TNF- $\alpha$ .
- These produce : an activation of the cytotoxic T-cells (CD8), macrophages, neutrophils, eosinophils, natural killer cells, and activation of antibody-dependent cell-mediated cytotoxicity,
- This is finally responsible for killing off virus infected cells or neoplastic cells and responsible for eliminating bacteria.

# Aim of the Studies

- ❑ To evaluate the effectiveness and safety of ozone therapy in hepatitis C genotype 4 infections
- ❑ To evaluate a proposed ozone therapy protocol in HCV genotype 4 treatment.
- ❑ Several studies and clinical observations were done within ten years from year 1999 to the year 2008.

# Patients and Methods

- ❑ One of the studies included 60 hepatitis "C" genotype 4 patients, 45 males and 15 females. Their age ranged between 34 and 65 years.
- ❑ Another study included 50 hepatitis "C" genotype 4 patients, 44 males and 6 females. Their age ranged between 23 and 58 years.
- ❑ Investigations including C.B.C., liver function tests, A.F.P., serological tests for Bilharziasis, P.C.R. quantitative for H.C.V., prothrombin time and concentration and abdominal ultrasonography were done before and 8 weeks, 24 weeks after starting treatment with ozone.

- ❑ First study: patients received combined MAH - dose range 4mg to 9 mg and RI - dose range 6mg to 14 mg per visit. Three visits / week for 8 weeks followed by 2/ week for 16 weeks.
- ❑ Second study : patients received combined MAH - dose range from 2.8 mg to 8.4 mg and RI - dose range from 6 mg to 12 mg per visit. Three visits / week for 12 weeks followed 2/ week for another 12 weeks.
- ❑ Investigations were repeated after 8 and 24 weeks of treatment. General health and daily activity were observed.



# Ozone Treatment Protocol

## First study:

- **MAH** 25 $\mu$ g/ml 2 successive times, then to 30 $\mu$ g/ml for another 2 times and so on, increasing the concentration by 5 $\mu$ g/ml every two sessions till reaching a maximum of 60  $\mu$ g/ml where this concentration was fixed till the end of treatment course. The volume was fixed at 150 ml. The blood weight was constant in each session at 150 gm.
- **RI** 20 $\mu$ g/ml with a volume of 300 ml 2 successive times, then increased to 25 $\mu$ g/ml with the same volume for another 2 successive times, then 30 $\mu$ g/ml x 300 ml twice, then 35 $\mu$ g/ml x 300 ml twice followed by 35 $\mu$ g/ml x 350 ml twice till we reach a maximum of 40 $\mu$ g/ml x 350 ml where this concentration and volume was fixed till the end of treatment.

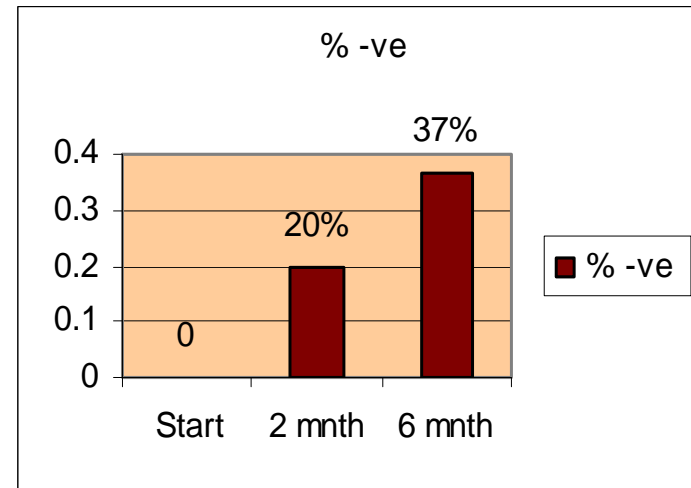
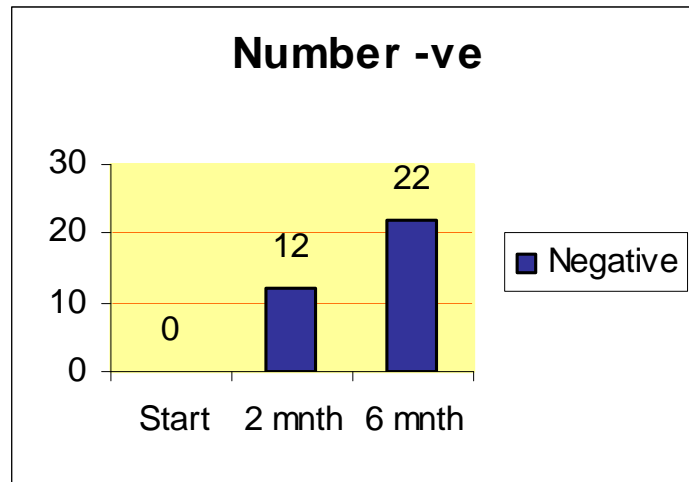
## Second study:

- **MAH** 20  $\mu\text{g/ml}$  2 successive times, then to 25  $\mu\text{g/ml}$  for 2 successive times and so on, increasing the concentration by 5 $\mu\text{g/ml}$  every 2 sessions till reaching a maximum of 60 $\mu\text{g/ml}$  were this concentration was fixed till the end of treatment course. Volume was fixed in all sessions at 140 ml. Blood weight was constant in each session at 140 gm.
- **RI** 15  $\mu\text{g/ml}$  with a volume of 250 ml for 2 successive times, then increased to 20  $\mu\text{g/ml}$  with the same volume for 2 successive times, then 25  $\mu\text{g/ml}$  x 250 ml twice, then 30  $\mu\text{g/ml}$  x 250 ml twice followed by 30  $\mu\text{g/ml}$  x 300 ml, then 35 $\mu\text{g/ml}$  x 300 ml twice till we reach a maximum of 40 $\mu\text{g/ml}$  x 300 ml were this concentration and volume was fixed till the end of treatment.

# RESULTS of FIRST STUDY

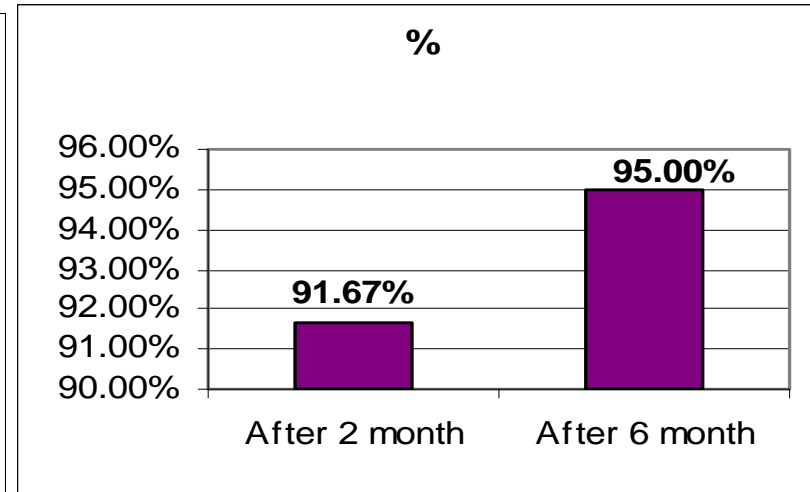
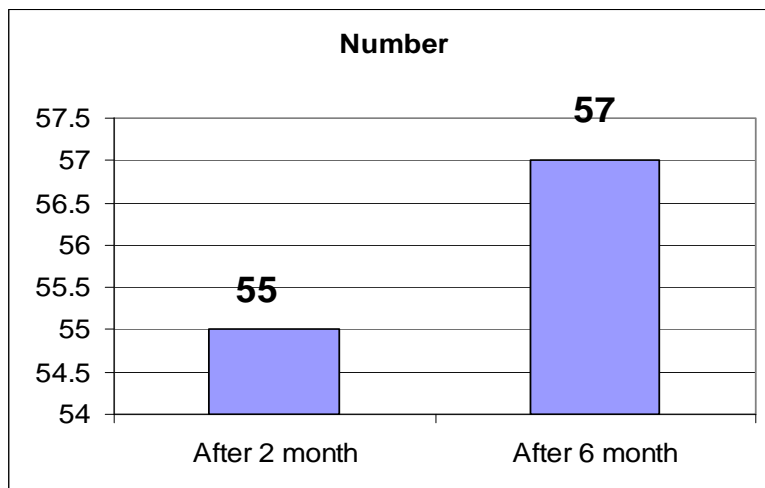
# PCR % -ve

	Number -ve	% -ve
After 2 Months	12	%20.00
After 6 Months	22	%36.67



# PCR % decline

	Number	%
After <b>2</b> Months	55	%91.67
After <b>6</b> Months	57	%95.00



# SGOT - AST

Number

Normal

Abnormal

Start

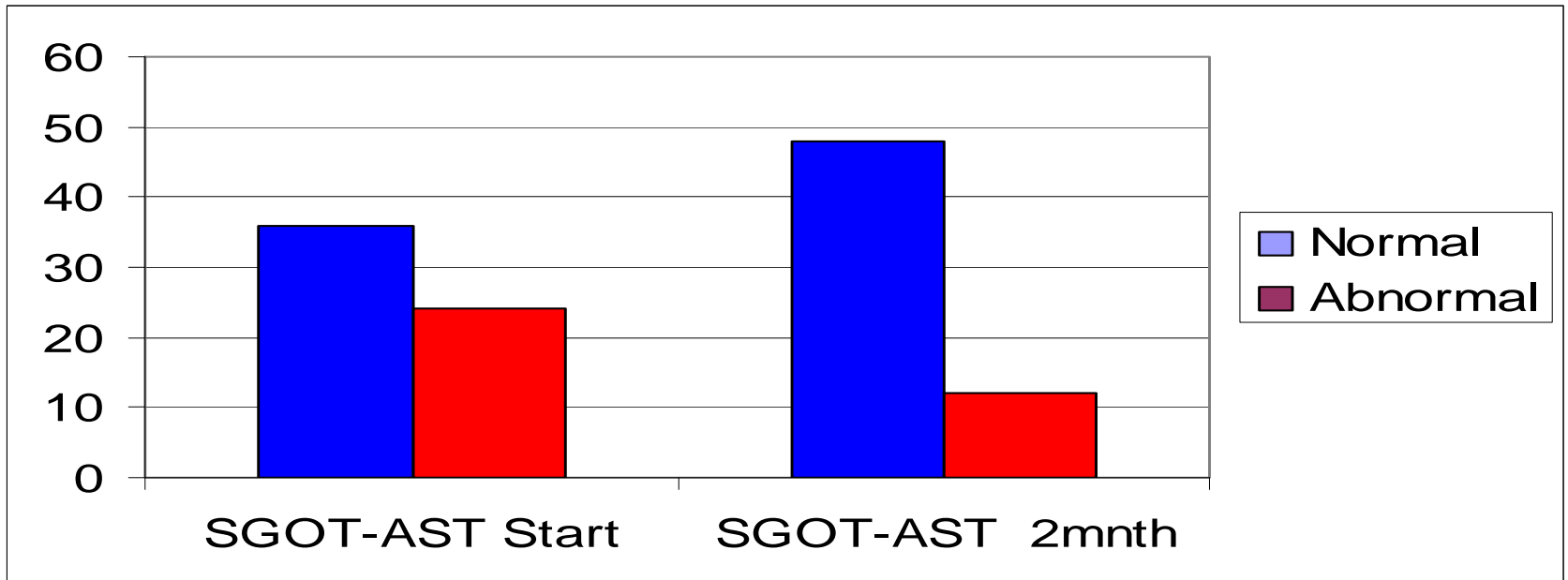
2 Month

36

48

24

12



# SGPT - ALT

Number

Normal

Abnormal

Start

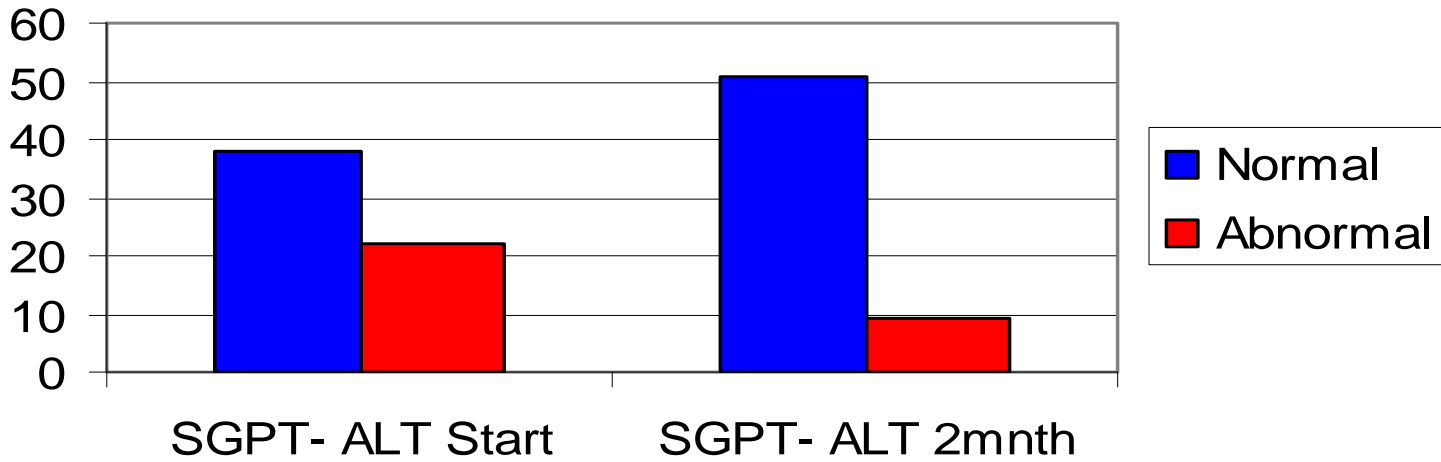
2 Month

38

51

22

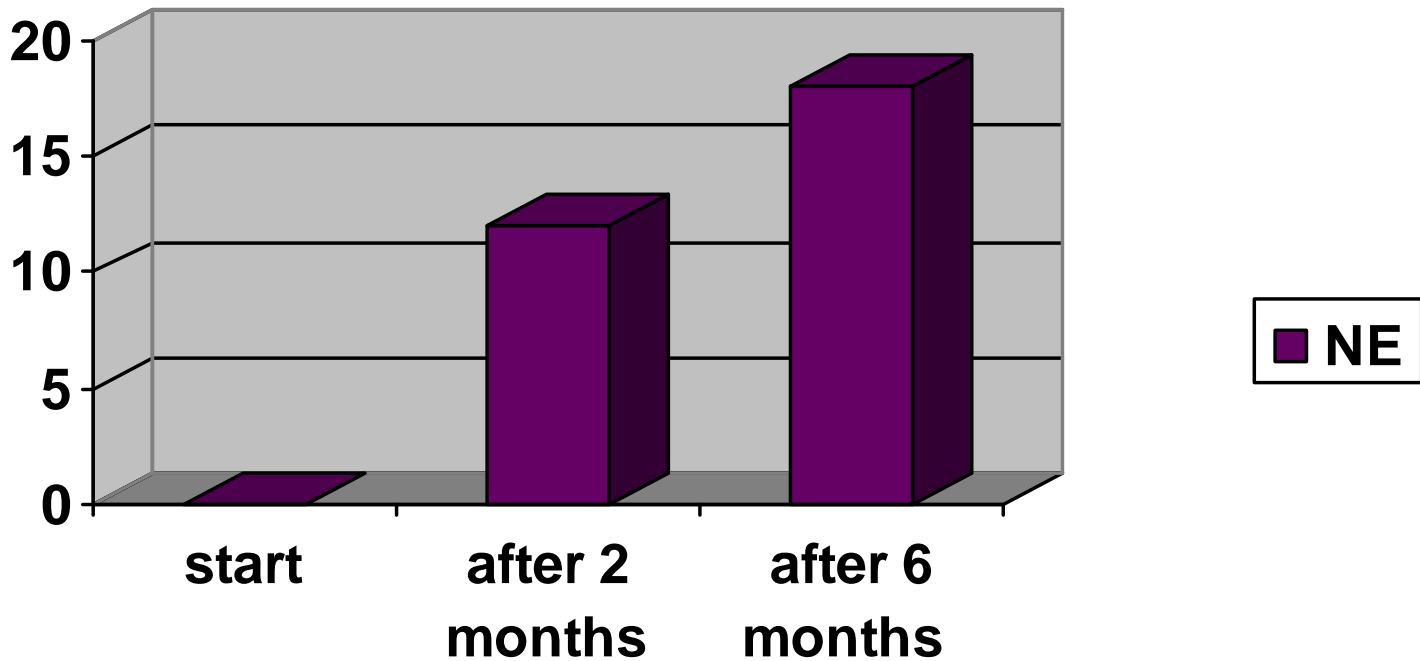
9



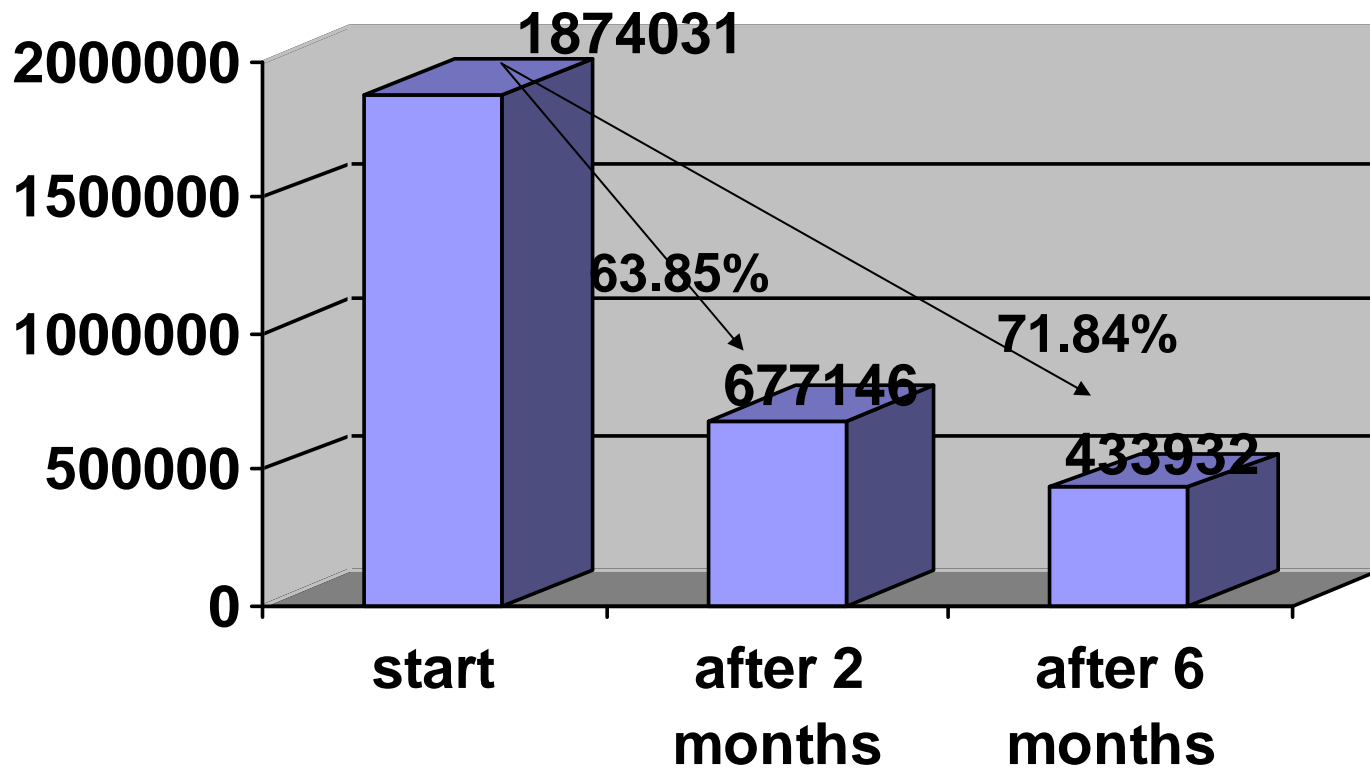
# RESULTS of SECOND STUDY



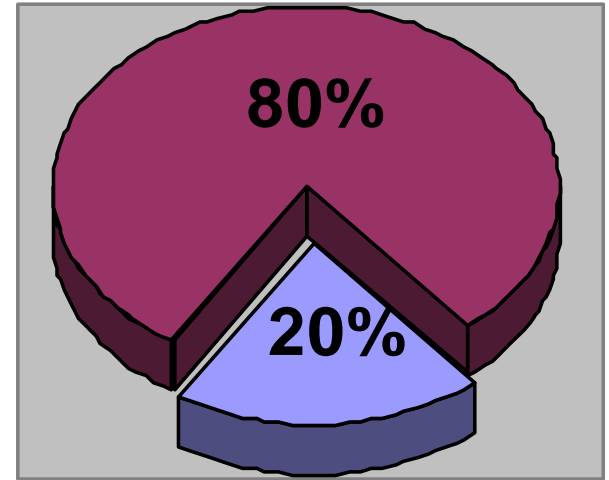
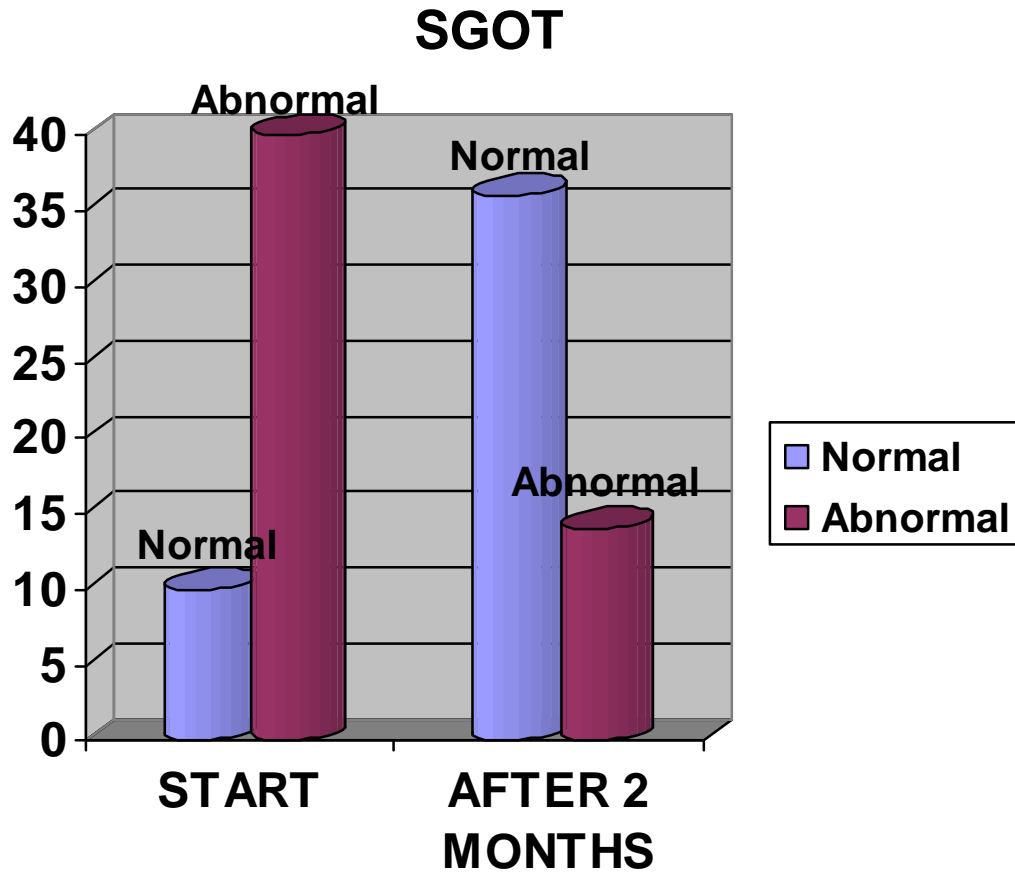
## Negative Viral load category before, during and after ozone therapy



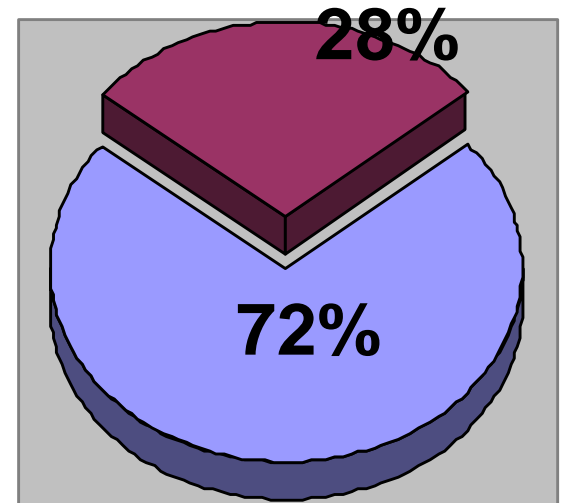
# PCR AVERAGES DECLINE



# SGOT BEFORE OZONE THERAPY

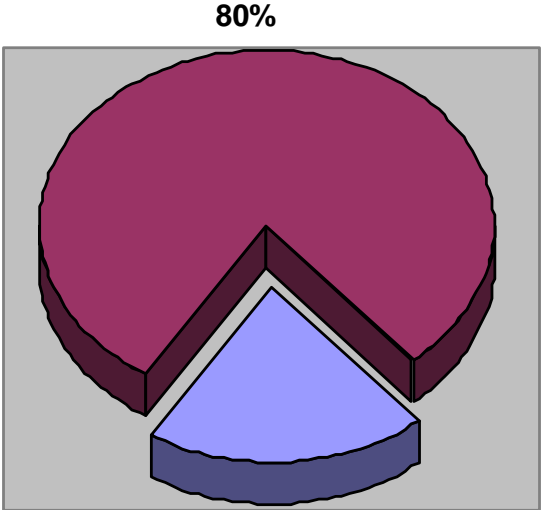
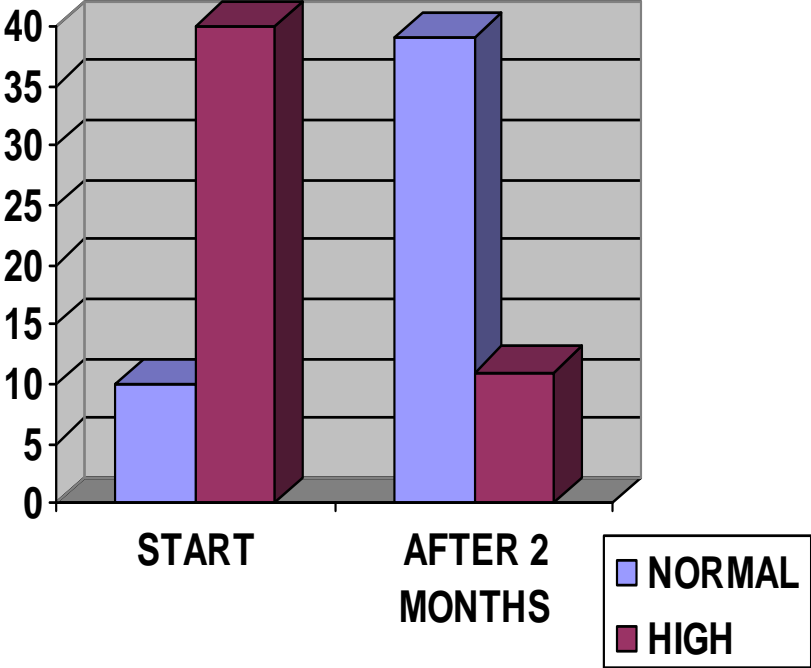


## SGOT AFTER 2 MONTHS

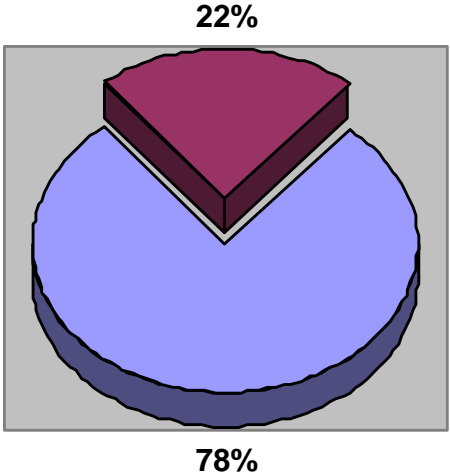


# SGPT BEFOR OZONE THERAPY

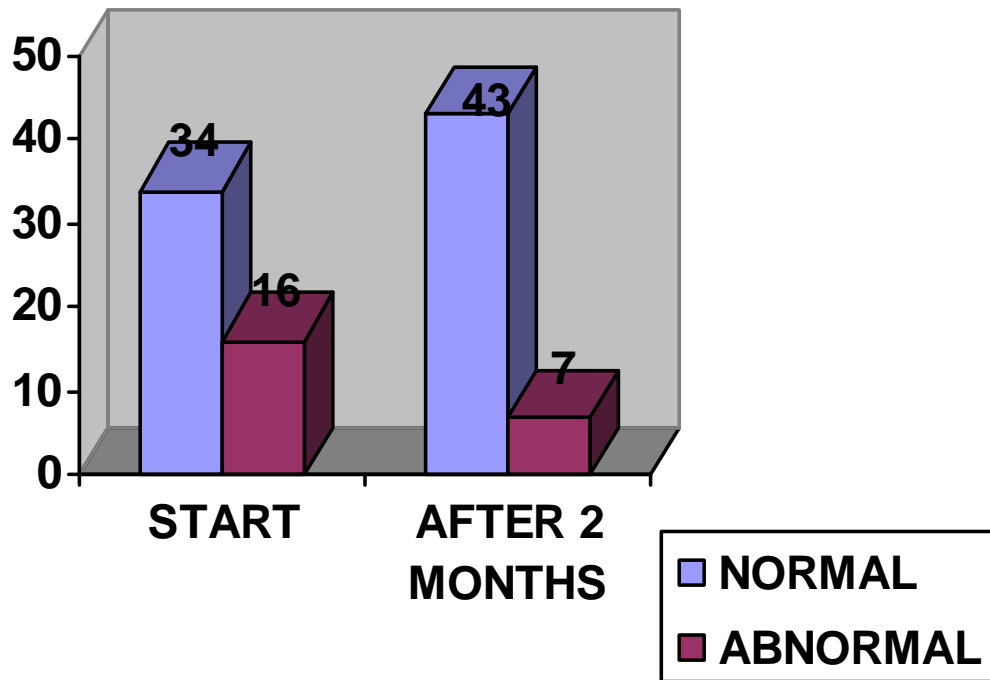
## SGPT



20%  
SGPT AFTER 2 MONTHS

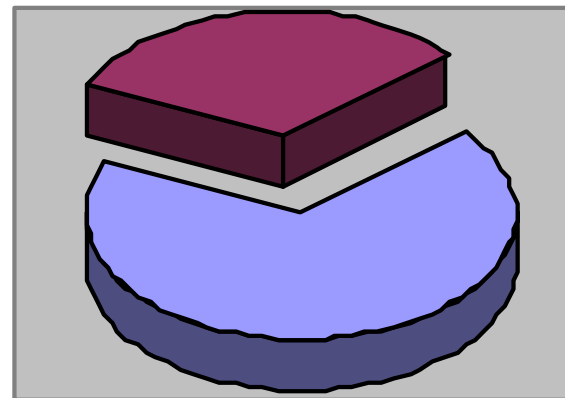


### ALBUMIN BEFOR OZONE THERAPY



### ALBUMIN BEFOR OZONE THERAPY

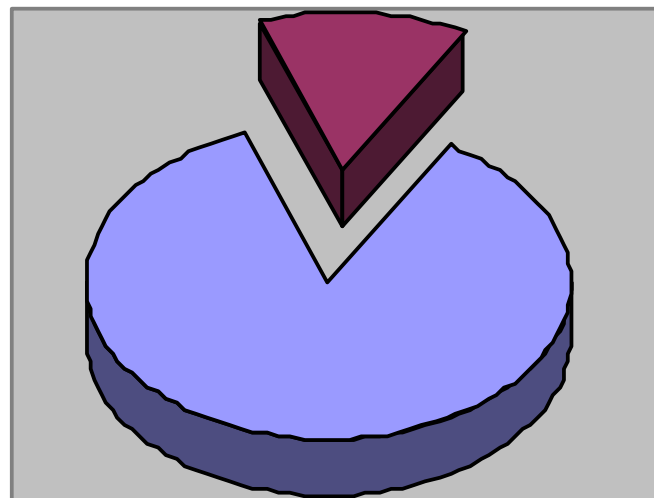
32%



68%

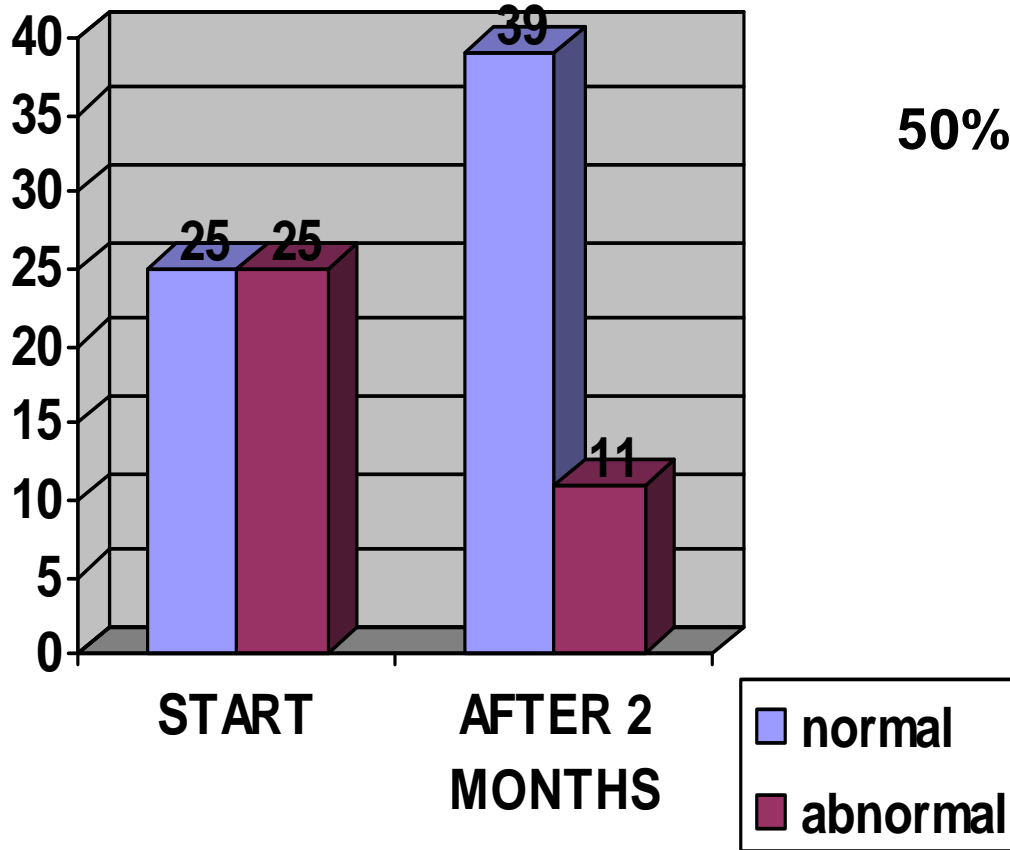
### ALBUMIN AFTER 2 MONTHES

14%

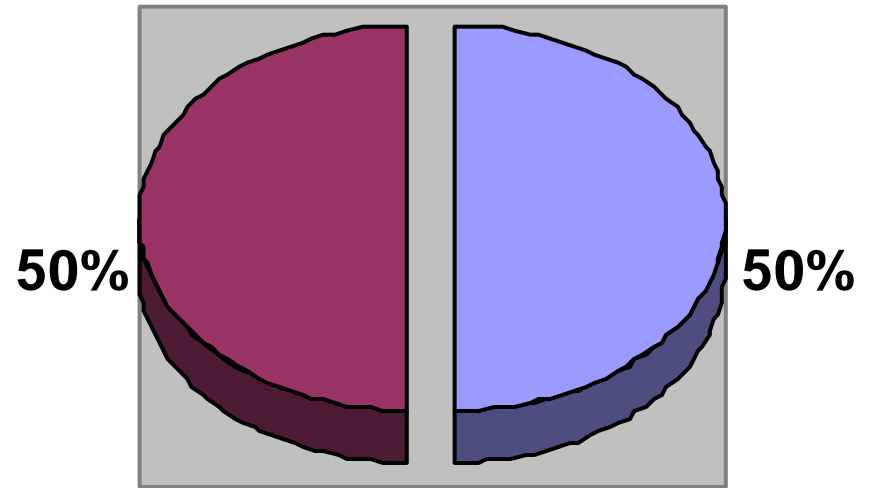


86%

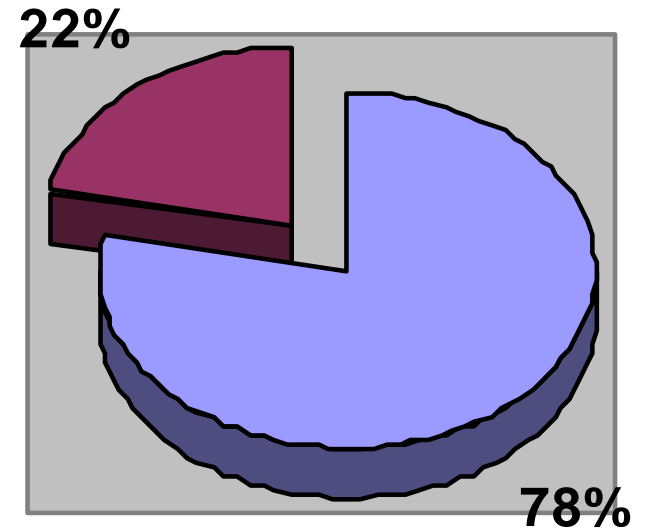
### BILIRUBIN



### BILIRUBIN BEFOR OZONE THERAPY



### BILIRUBIN AFTER 2 MONTHES



# OTHER RESEARCHES

- ❑ A third research on 30 HCV genotype 4 patients performed in a different center gave almost the same results like the first two researches.
- ❑ Combination of interferon administration and ozone therapy in four HCV type 4 patients gave better results than either one of them alone with less side effects of interferon
- ❑ One year follow-up of HCV cases treated with ozone therapy for 6 months revealed that there was a relapse rate of approximately 40%. However the liver function tests were not affected denoting that the relapsed virus had little effect on the liver.

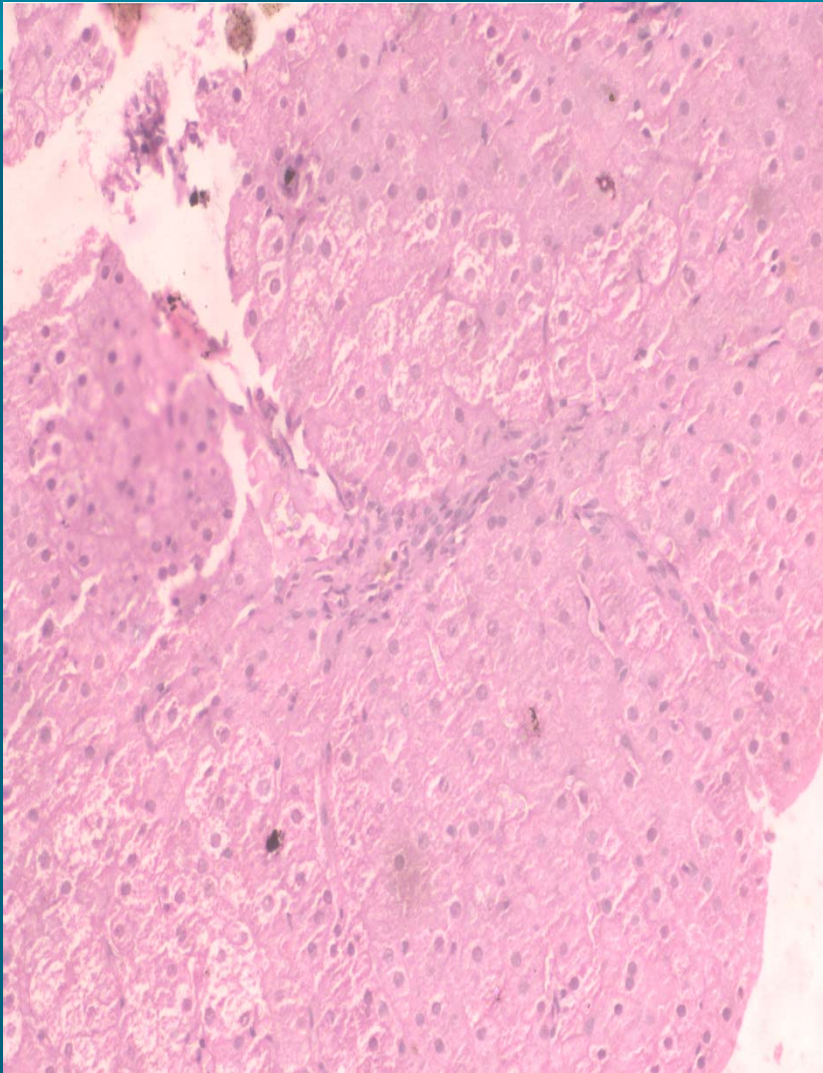


❑ From the previous researches we found that ozone therapy has a positive effect on the liver function tests even in late stages with liver cirrhosis where interferon is contraindicated.

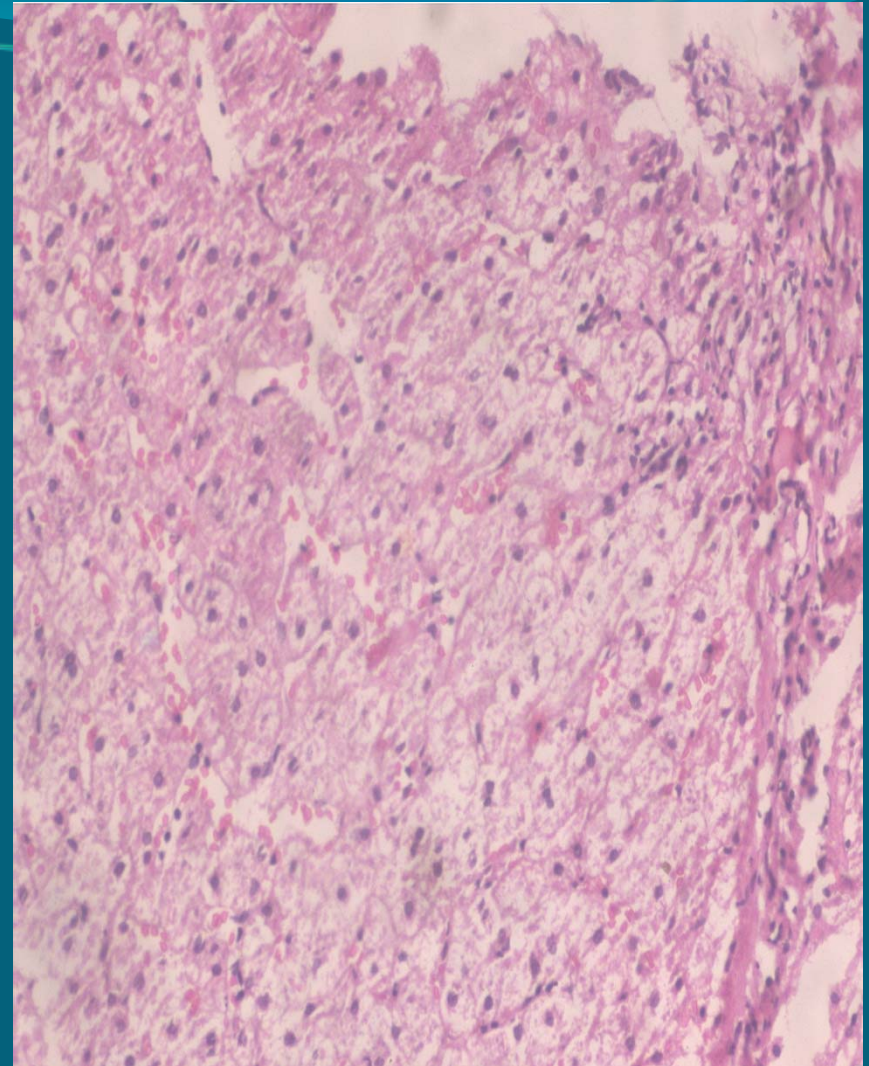
❑ The effect of ozone on the HCV infected blood units was studied. Medical ozone was bubbled through the infected blood units with different concentrations ranging from 20 to 50  $\mu$ /ml for 5 successive days. There was no statistically significant decrease in the HCV viral load.

A histo-pathological study was done by Elbasha H. et al. in the year 2006 performed on 98 HCV patients in Egypt to evaluate the effect of ozone therapy on the liver tissue in 12 weeks therapy period. They came to the conclusion that:

- ❑ Ozone therapy induces downgrading in necro-inflammatory changes in liver biopsy by 2-8 points.
- ❑ Ozone therapy induced down staging in fibrosis by 1-2 points in 65 – 82.5 % of cases



Before treatment 8/18 grade of  
inflammation  
3/6 Stage of fibrosis H&E, X200



After treatment 4/18 grade of  
inflammation,  
0/6 *stage of fibrosis H&E, X200*

# Discussion

□ The significant decrease in viral load is an important factor – among other factors – for judging the improvement of a case of hepatitis C virus. In these studies, it was found that following ozone therapy; there was a significant reduction of viral load. This decrease was evident after 8 weeks and further decline following another 16 weeks of ozone therapy.

□ Normal enzyme levels are a very important indicator denoting the sound integrity of liver cells. In these studies, it was found that following ozone therapy; there was a significant change of abnormal enzyme levels towards normal values.

□ One of the major important parameters that signify liver function are the bilirubin and albumin levels. In the second study it was found that both parameters were improved and back to normal with a statistically significant readings denoting liver function improvement.



❑ One histo-pathological study proved that ozone therapy has an anti-inflammatory and anti-fibrotic effect on the liver of HCV patients. This proves the beneficial effect of ozone therapy on the integrity of liver tissue.

❑ Clinical observations and questioning of the patients revealed that in more than 90 % of cases the general condition improved and some of patients returned to work after they were staying at home. Moreover in most cases there were improvement of the quality of life and they had the sense of well-being. All the previous data; points to the important role of ozone a safe, effective method of therapy.

❑ Not only ozone was effective in managing HCV cases, but also it had a therapeutic effect on some associated conditions e.g. diabetes, hypertension and prostatic enlargement.

❑ These researches signifies that ozone therapy has a positive effect on the liver function tests even in late stages with liver cirrhosis where interferon is contraindicated

❑ In spite of the high percentage of relapse (+ve PCR) observed following ozone therapy, it had little effect on the liver function tests. This means that quantitative PCR is not a major factor for evaluation of liver performance; but only one factor among others.

❑ It was found by a preliminary research that there was no significant decrease in the HCV viral load following exposing the HCV infected blood units to medical ozone. This suggests that the main effect of ozone therapy on the virus is due to its immune-stimulating effect rather than a direct antiviral effect.

# Conclusion

Ozone therapy was found to be an effective, safe and less expensive method in Hepatitis "C" genotype 4 patients. It can be used safely even if there is a complication or associated disease.



# Recommendations

- ❑ A double blind randomized placebo controlled study. The patients must be selected with no complications (cirrhosis, ascitis, liver cell failure, etc..) and no associated chronic disease (Diabetes, Bilharziasis, etc..) Considering the high relapse rate following ozone therapy; this study should be a long-term study for one year and the follow-up by observation and investigations for another year.
- ❑ A study with large number of patients to evaluate the efficacy of combination of interferon administration and ozone therapy in HCV genotype 4 patients and to evaluate the possible role of ozone in increasing the efficacy, and diminishing both the side effects and course duration of interferon therapy.

# Recommendations (cont.)

- The new studies should be on the basis of the low dose concept due to its safety and its major beneficial effect on the immune system
- An extensive study on the effect of frequent exposure of HCV infected blood units to medical ozone is recommended.



**Thank You**