RESULTS

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The results of the present study are presented in the tables (from table 19 to table 27) and in the figures (from figure 14 to figure 26).

Table (19) shows the mean valve ± standard deviation (std. dev.), and the range of serum TNF-α in the reference group and in the first and second samples of chronic liver disease and hepatitis E virus (HEV) +ve groups.

In the reference group, the mean value ± std. dev. of serum TNF-α was 51.6 ± 30 pg/ml and the range was 13-116 pg/ml.

Of the 20 sera from apparently healthy children, 18 (90%) had serum TNF-α levels ≤ 80 pg/ml (the range was 13-80 pg/ml) and 2 (10%) had serum TNF-α levels > 80 pg/ml (100 and 116 pg/ml).

Figure (14) shows the correlation between serum TNF-α level and age in the reference group.

There was a significant negative correlation between age and serum TNF-α level in the reference group at $p<0.05$ and correlation coefficient $(r) = -0.489$.

However, there was no correlation between serum TNF-α level and sex in the reference group.

Figure (15) shows serum TNF-α levels in the reference group, first and second samples of chronic liver disease and hepatitis E virus + ve groups.

In the chronic liver disease group, the mean value ± std. dev. of serum TNF-α in the first samples was 152.9 ± 49.7 pg/ml and the range was 75-320 pg/ml, whereas in the second samples, the mean value ± std.dev. of serum TNF-α was 205 ± 65.7 pg/ml and the range was 100-400 pg/ml.

In the hepatitis E virus (HEV) + ve group, the mean value ± std. dev. of serum TNF-α in the first samples was 192.2 ± 126.7 pg/ml and the range was 65-360 pg/ml, while in the second samples, the mean value ± std. dev. of serum TNF-α was 217.9 ± 159.6 pg/ml and the range was 16-380 pg/ml.

There was a significant difference in serum TNF-α level between the reference group and the first samples of chronic liver disease and HEV+ve groups at $p<0.001$. However, there was no significant difference in TNF-α level between the first samples of chronic liver disease and HEV + ve groups.

Also, there was no significant difference in serum TNF-α level in the second samples between the chronic liver disease and HEV + ve groups.

In chronic liver disease group, there was a significant difference in serum TNF-α level between the second and first samples at $p<0.0001$.

In HEV+ve group, there was also a significant difference in serum TNF-α level between the second and first samples at $P<0.02$.

Table (23) shows the differences in the liver function tests between the second samples of chronic liver disease and HEV+ve groups.

Table (24) shows the differences in the liver function tests between the first and second samples in the chronic liver disease group.

Table (25) shows the differences in the liver function tests between the first and second samples in HEV+ve group.

Table (26) shows the rate (%) of change of liver function tests in the chronic liver disease and HEV+ve groups.

Figure (16) shows the mean value ± std.dev. of serum AST in reference group, first and second samples of chronic liver disease and HEV+ve groups.

There was a significant difference in serum AST level between the first sample of chronic liver disease group and the other 2 groups at $P<0.0001$, but there was no significant difference in the serum AST level between the reference group and the first sample of HEV+ve groups.

There was a significant difference in the serum AST level between the second samples of chronic liver disease and HEV+ve groups at $P<0.01$

In the chronic liver disease group, there was a significant difference in the serum AST level between the second and first samples at $P< 0.001$.

In the HEV+ve group, there was also a significant difference in the serum AST level between the second and first samples at P<0.0008.

However, the chronic liver disease group showed a significantly higher rate of increase in the serum AST level (43.6%) than the HEV+ve group (21.5%) at P<0.03.

Figure (17) shows the mean value ± std.dev. of serum ALT in reference group, first and second samples of chronic liver disease and HEV+ve groups. There was a significant difference in the serum ALT level between the reference group and the first samples of chronic liver disease and HEV+ve groups at P<0.0005, but there was no significant difference in its level between the first samples of chronic liver disease and HEV+ve groups.

There was no significant difference in the serum ALT level between the second samples of chronic liver disease and HEV+ve groups.

In the chronic liver disease group, there was a significant difference in the serum ALT level between the second and first samples at P<0.007.

In HEV+ve group, there was a significant difference in the serum ALT level between the second and the first samples at P<0.002.

However, the chronic liver disease group showed a significant higher rate of increase in serum ALT (53.2%) than the HEV+ve group (23.5%) at P<0.03.

Figure (18) shows the mean value ± std.dev. of serum alkaline phosphatase in the reference group, first and second samples of chronic liver disease and HEV+ve groups.

There was a significant difference in the serum alkaline phosphatase level between the reference group and the first samples of the other 2 groups at $P<0.0001$, also, there was a significant difference in its level between the first samples of chronic liver disease and HEV+ve groups at $P<0.0001$.

There was a significant difference at $P<0.003$ in the serum alkaline phosphatase level between the second samples of chronic liver disease and HEV+ve groups.

In chronic liver disease group, there was a significant difference in serum alkaline phosphatase level between the second and first samples at $P<0.008$.

In HEV+ve group, there was a significant difference in the serum alkaline phosphatase level between the two samples at $P<0.0001$.
However, there was no significant rate of change in serum alkaline phosphatase between the two groups.

Figure (19) shows the mean value ± std.dev. of total serum bilirubin in the reference group, first and second samples of chronic liver disease and HEV +ve groups.

There was no significant difference in the total serum bilirubin level between the reference group and the first samples of chronic liver disease and HEV +ve groups. Also it showed no significant difference between the second samples of chronic liver disease and HEV +ve groups.

As regards the difference in total serum bilirubin level between the second and first samples of chronic liver disease group, it was non significant, whereas in HEV +ve group, it showed a significant difference between the second and first samples at $P<0.0003$. However, there was no significant rate of change in total serum bilirubin level between the two groups.

Figure (20) shows the mean value ± std.dev. of serum direct bilirubin in the reference group, first and second samples of chronic liver disease and HEV+ve groups.

There was no significant difference in serum direct bilirubin level between the reference group and the first samples of the other 2 groups, also there was no significant difference in its level between the first samples and between the second samples of chronic liver disease and HEV +ve groups.

In the chronic liver disease group, serum direct bilirubin showed no significant difference between the first and the second samples whereas, in HEV +ve group, it showed a significant difference between the first and the second samples at $P<0.0003$.

However, it showed no significant rate of change between the two groups.

Figure (21) shows the mean value ± std.dev. of total serum protein in the reference group, first and second samples of chronic liver disease and HEV +ve groups.

Total serum protein showed no significant difference in its level between the reference group, and the first samples of the other 2 groups. Also, it showed no significant difference in its level between the first samples and between the second samples of chronic liver disease and HEV +ve groups.

In the chronic liver disease group, there was no significant difference in total serum protein between the first and second samples, however, in HEV+ve group, it showed a significant difference in its level between the first and the second samples at $P<0.0001$.

The HEV +ve group showed a significant higher rate of increase in the total serum protein level (2.0%) than the chronic liver disease group (0.38%) at $P<0.01$.

Figure (22) shows the mean value ± std. dev. of serum albumin in the reference group, first and second samples of chronic liver disease and HEV +ve groups.

There was a significant difference in serum albumin level between the frist sample of the chronic liver disease group and the other 2 groups at

P<0.001, but there was no significant difference in its level between the reference group and the first sample of HEV +ve group.

Also, there was a significant difference in serum albumin level between the second samples of chronic liver disease and HEV +ve groups at P<0.001. In the chronic liver disease group, serum albumin showed a significant difference between the first and second samples at P<0.0001.

In HEV +ve group, at P<0.0001, serum albumin showed a significant difference between the first and the second samples.

At P<0.01, the chronic liver disease group showed a significantly larger rate of decrease in the serum albumin level (-7.3%) than the HEV+ve group (-4.2%).

Figure (23) shows the mean value ± std.dev. of A/G ratio in the reference group, first and second samples of chronic liver disease and HEV +ve group.

The A/G ratio showed a significant difference in its level between the reference group and the first samples of the other 2 groups at P<0.0001, also there was a significant difference in the ratio between the first samples of chronic liver disease group and HEV +ve group at P<0.0001.

At P<0.002, there was a significant difference in A/G ratio between the second samples of chronic liver disease and HEV +ve groups.

In the chronic liver disease group, there was a significant difference in A/G ratio between the first and second samples at P<0.0001.

In HEV +ve group there was also a significant difference in A/G ratio between the 2 samples at P<0.0001, however, the chronic liver disease group showed a significantly larger rate of decrease in A/G ratio (-12.5%) than the HEV+ve group (-5.7%) at P<0.0002.

Figure (24) shows the mean value ± std.dev. of prothrombin time in the reference group, first and second samples of chronic liver disease and HEV +ve groups.

There was no significant difference in the prothrombin time between the reference group and the first samples of chronic liver disease and HEV +ve groups, also, it ahowed no significant difference between the first samples of chronic liver disease and HEV +ve groups. However, there was a significnat difference in prothrombin time between the second samples of chronic liver disease and HEV +Ve groups at P<0.03.

In the chronic liver disease group, there was a significant difference in the prothrombin time between the first and second samples at P<0.0001.

In HEV +ve group, the prothrombin time also showed a significant difference between the 2 samples at P<0.0001, but the chronic liver disease group showed a significantly higher rate of increase in prothrombin time (4.3%) than the HEV +ve group (2.8%) at P<0.02.

Figure (25) shows prothrombin concentration in the reference group, first and second samples of chronic liver disease and HEV +ve groups.

There was no significant difference in prothrombin concentration between the reference group and the first samples of the other 2 groups, also, it showed no significnat difference between the first samples of chronic liver disease and HEV +ve groups. On the other hand, we found a significant difference in prothrombin concentration between the second samples of chronic liver disease and HEV +ve groups at $P<0.006$.

In the chronic liver disease group, there was a significant difference in prothrombin concentration between the 2 samples at $P<0.0001$.

In HEV +ve group, prothrombin concentration also showed a significant difference between the first and second samples at $P<0.0001$, however, the chronic liver disease group showed a significantly larger rate of decrease in prothrombin concentration (-8.8%) than the HEV +ve group (-6.1%) at $P<0.04$.

As regarads the correlations between the rate of change of serum TNF-α and the rate of change of the liver function tests in the chronic liver disease group, there was no significant correlation between the rate of increase of serum TNF-α and the following:

* The rate of increase in the serum AST level.
* The rate of increase in the serum ALT level.
* The rate of increase in the serum alkaline phosphatase level.

* The rate of increase in the total serum bilirubin and serum direct bilirubin levels.
* The rate of increase in the total serum protein level.
* The rate of decrease in the serum albumin level and A/G ratio.
* The rate of increase in the prothrombin time and the rate of decrease in the prothrombin concentration.

Also, in the hepatitis E virus +ve group, the rate of increase in the serum TNF-α level showed no significant correlation with most of the liver function tests.

When the patients suffering from chronic liver disease were segregated according to the histopathological findings in the liver biopsy into the following groups:

* Glycogen storage disease group.
* Chronic persistent hepatitis group.
* Bilharzial portal fibrosis group.
* Bilharzial portal fibrosis and chronic active hepatitis (mixed) group.
* Posthepatitic micronodular cirrhosis.
* Intrahepatic biliary cirrhosis, no significant correlation could be proved between the serum TNF-α levels (the first sample, or the second sample or the rate of increase in serum TNF-α) and the histopathological findings in the liver biosy. However, it is worthwhile to mention that, cases of bilharzial portal fibrosis and cases of liver cirrhosis showed a remarkably elevated serum TNF-α levels.

Table (27) and figure (26) show the different cut off levels of serum TNF-α and the corresponding specificity and sensitivity values of each level.

This is testing the reliability of the different cut off levels of serum TNF-α (the second sample) in picking up the chronic liver conditions through the sensitivity and specificity. The optimum sensitivity (75%) and specificity (78.6%) lie between 188.8-200 pg/ml TNF-α. Therefore, this range will be considered the cut off value of serum TNF-α.

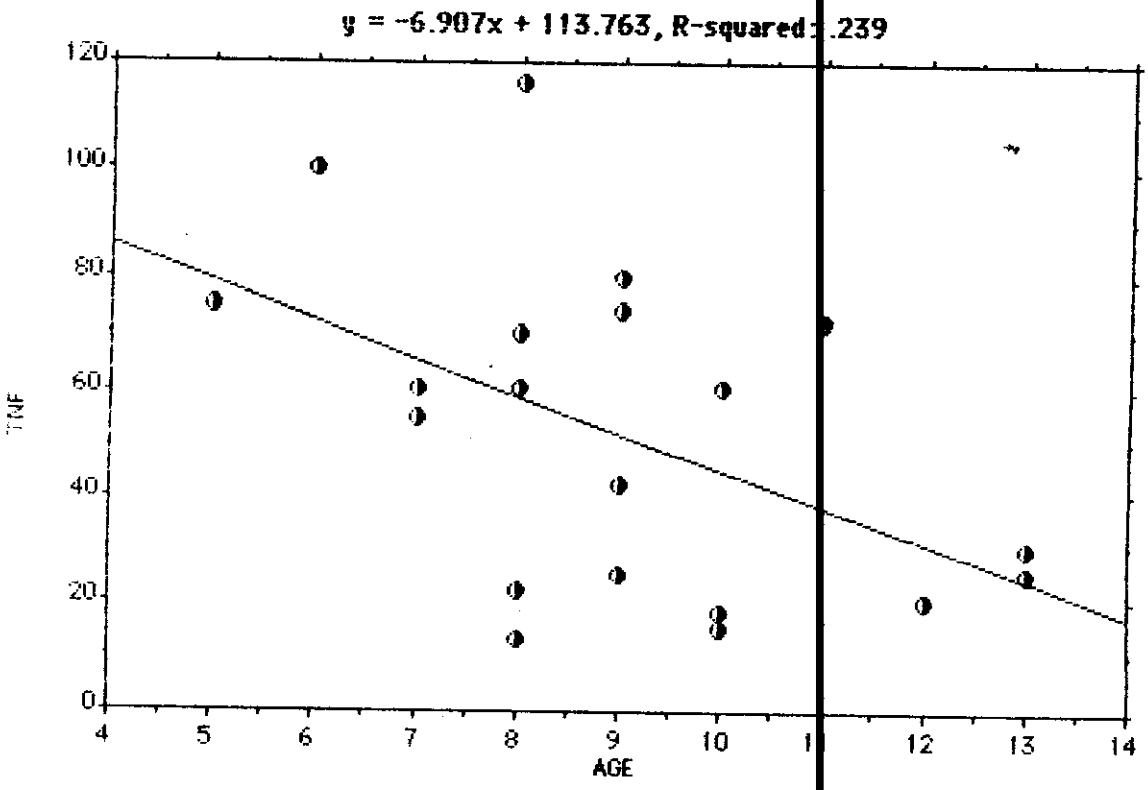

Figure (14): The correlation between serum TNF-α levels and age in the reference group.

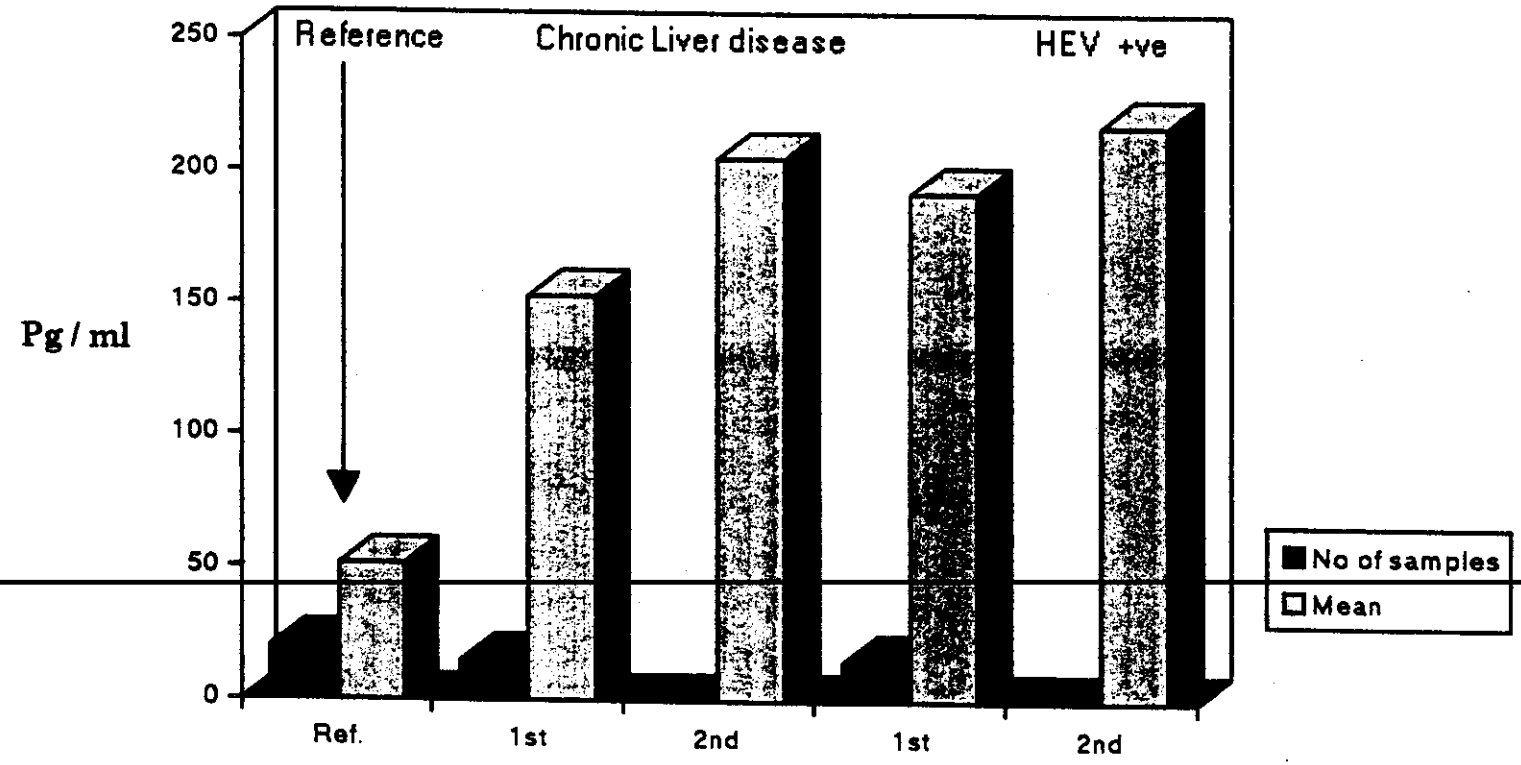

Figure (15): Serum TNF -α in the reference group, first and second samples of chronic liver disease and hepatitis E virus +ve groups.

Table (20): The incidence of elevation of serum TNF-alpha in the reference group and in the first and second samples of chronic liver disease and HEV +ve groups.

		Serum TNF-alpha ranges pg/ml	
Group	No. of cases	13:80	>80
Reference	20	18/20(90%)	2/20(10%)
Chronic liver disease	15		
1st sample		1/15(6.6%)	14/15(93.4%)
2nd sample		0/15	15/15(100%)
Hepatitis E virus +ve	15		
1st sample		3/15(20%)	12/15(80%)
2nd sample		2/15(13.3%)	13/15(86.7%)

Table (21): The rate of change (increase) of serum TNF-alpha in chronic liver disease and hepatitis E virus +ve groups.

Group	No. of cases	Mean Pg/ml	Std dev. Pg/ml
Chronic liver disease	15	35.5	18.8
Hepatitis E virus +ve	15	8.5	27.6

Table (22): The differences in the liver function tests between the reference group and the first samples of chronic liver disease and hepatitis E virus +ve groups.

Liver function test			Group and No. of cases			
	Reference		Chronic liver disease		Hepatitis E virus +ve	
	20		15		15	
	Mean	Std.dev	Mean	Std.dev	Mean	Std.dev.
AST (U/l)	7.4	19	52.7	45.7	24.6	16.9
ALT (U/l)	7.8	1.5	27.9	23	17.9	11.2
Alkaline phosp-hatase (K &K)	13.35	1.7	23	4.8	16	3.1
Total serum bilirubin (mg%)	0.71	0.13	2.5	0.47	1.3	0.74
Serum direct bilirubin (mg%)	0.19	0.16	1.2	0.39	0.8	0.5
Total serum protein (g/l)	6.9	1.2	7.2	0.46	7.7	0.19
Serum albumin (g/l)	4.9	0.37	4	0.64	4.6	0.34
A/G Ratio	1.69	0.17	1.25	0.29	1.47	0.22
Prothrombin time (sec.)	12.7	0.6	13.1	0.8	12.7	0.5
Prothrombin concentration (%)	87.7	9.3	80.8	10	88.4	8.9

Table (23): The differences in the liver function tests between the second samples of chronic liver disease group and hepatitis E virus +ve group.

Liver function test	Group and No.of cases			
	Chronic liver disease		Hepatitis E virus +ve	
	15		15	
	Mean	Std.dev	Mean	Std.dev
AST (U/l)	70.9	55.3	30.4	21.7
ALT (U/l)	43.5	40.5	22.6	15.7
Alkaline phosph-atase (K&K)	26.2	6.9	18.3	3.6
Total serum bilirubin (mg%)	2.9	0.37	1.5	0.8
Serum direct bilirubin (mg%)	1.4	0.7	0.9	0.7
Total serum protein (g/l)	7.3	0.5	7.8	0.2
Serum albumin (g/l)	3.7	0.6	4.4	0.4
A/G Ratio	1.1	0.27	1.4	0.21
Prothrombin time (sec.)	13.7	0.9	13	0.6
Prothrombin concentration (%)	73.6	8.6	8.3	8.9

Table (24): The differences in the liver function tests in the chronic liver disease group between the first and second samples.

Liver function test	First sample		Second sample	
	Mean	Std.dev	Mean	Std.dev
AST (U/l)	52.7	45.7	70.9	55.3
ALT (U/l)	27.9	23	43.5	40.5
Alkaline phosp-hatase (K&K)	18.2	4.8	25.1	2.9
Total serum bilirubin (mg%)	2.7	0.47	2.6	0.37
Serum direct bilirubin (mg%)	1.4	0.39	1.2	0.7
Total serum protein (g/l)	7.2	0.46	7.1	0.5
Serum albumin (g/l)	4	0.64	3.7	0.6
A/G Ratio	1.25	0.29	1.1	0.27
Prothrombin time (sec.)	13.1	0.8	13.7	0.9
Prothrombin concentration (%)	80.8	10	73.6	8.6

Table (25): The differences in the liver function tests in the hepatitis E virus +ve group between the first and second samples.

Liver function test	First sample		Second sample	
	Mean	Std.dev	Mean	Std.dev
AST (U/l)	24.6	16.9	30.4	21.7
ALT (U/l)	17.9	11.2	22.6	15.7
Alkaline phosp-hatase (K&K)	15.5	3.1	18.2	3.6
Total serum bilirubin (mg%)	1.3	0.74	1.5	0.8
Serum direct bilirubin (mg%)	0.8	0.5	0.9	0.7
Total serum protein (g/l)	7.7	0.19	7.6	0.2
Serum albumin (g/l)	4.6	0.34	4.4	0.4
A/G Ratio	1.47	0.22	1.4	0.21
Prothrombin time (sec.)	12.7	0.5	13	0.6
Prothrombin concentration (%)	88.4	8.9	83	8.9

Table (26): The rate (%) of change of liver function tests in the chronic liver disease and hepatitis E virus +ve groups.

Liver function test	Group and No.of cases			
	Chronic liver disease		Hepatitis E virus +ve	
	15		15	
Rate of change	Mean	Std.dev.	Mean	Std.dev
AST (U/l)	43.6	38	21.5	8.5
ALT (U/l)	53.2	49.9	23.5	10.3
Alkaline phosph-atase (K&K)	17.3	20.5	17	10.4
Total serum bilirubin (mg%)	6.7	20.9	13.2	12.3
Serum direct bilirubin (mg%)	21.6	38.7	13.2	11
Total serum protein (g/l)	0.38	2.1	2	1.5
Serum albumin (g/l)	-7.3	3.9	-4.2	1.9
A/G Ratio	-12.5	5.6	-5.7	2.4
Prothrombin time (sec.)	4.3	1.8	2.8	1.4
Prothrombin concentration (%)	-8.8	3.8	-6.1	2.8

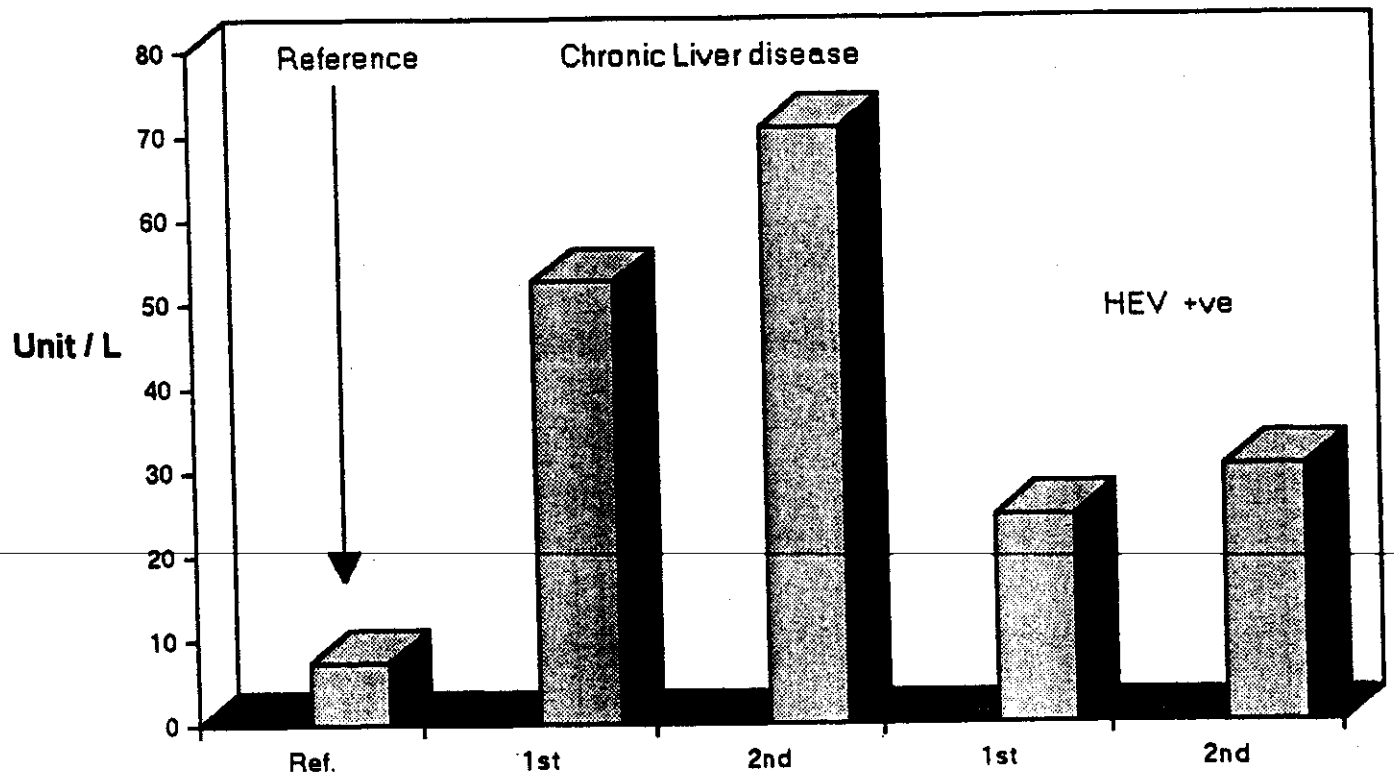

Figure (16): Serum AST in the reference group, first and second samples of chronic liver disease and hepatitis E virus +ve groups.

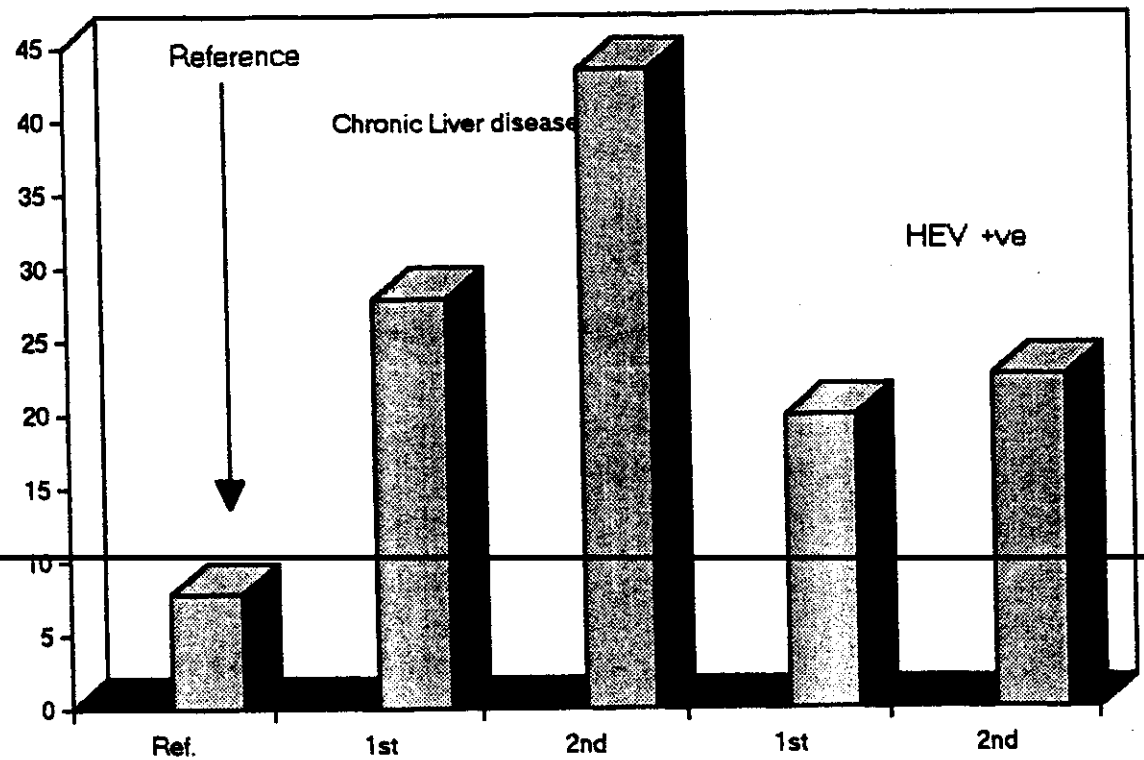

Figure (17): Serum ALT in the reference group, first and second samples of chronic liver disease and hepatitis E virus +ve groups.

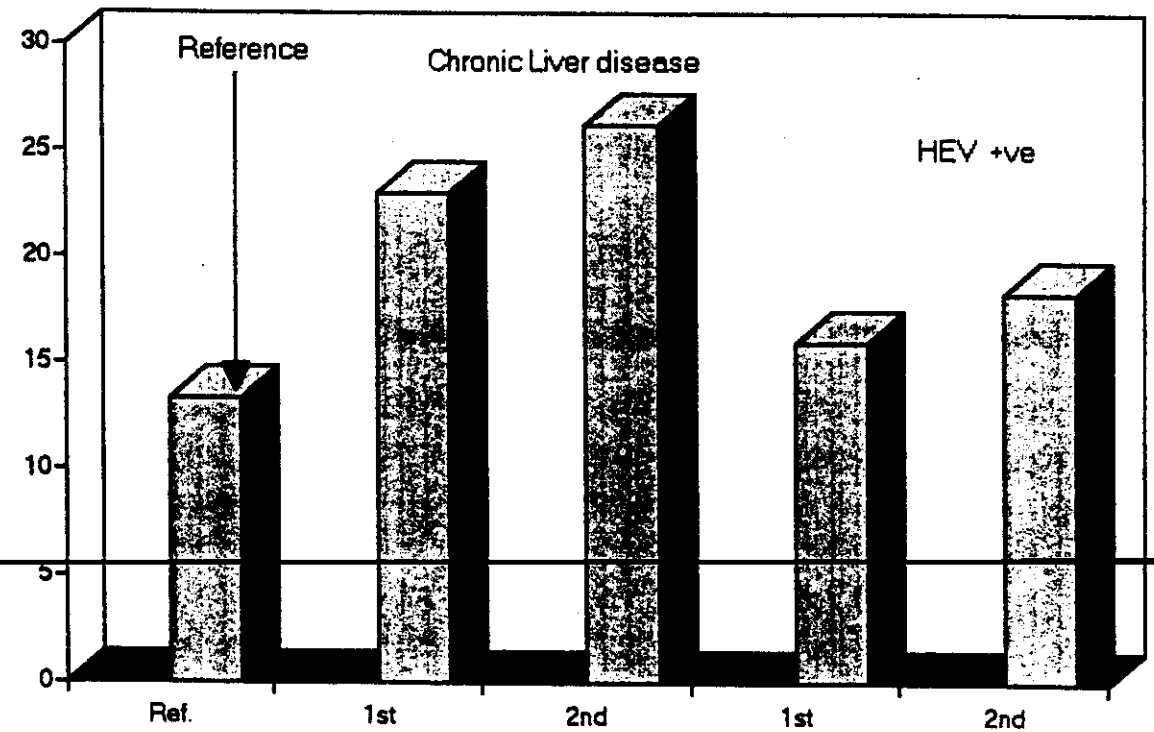

Figure (18): Serum alkaline phosphatase in the reference group, first and second samples of chronic liver disease and hepatitis E virus +ve groups.

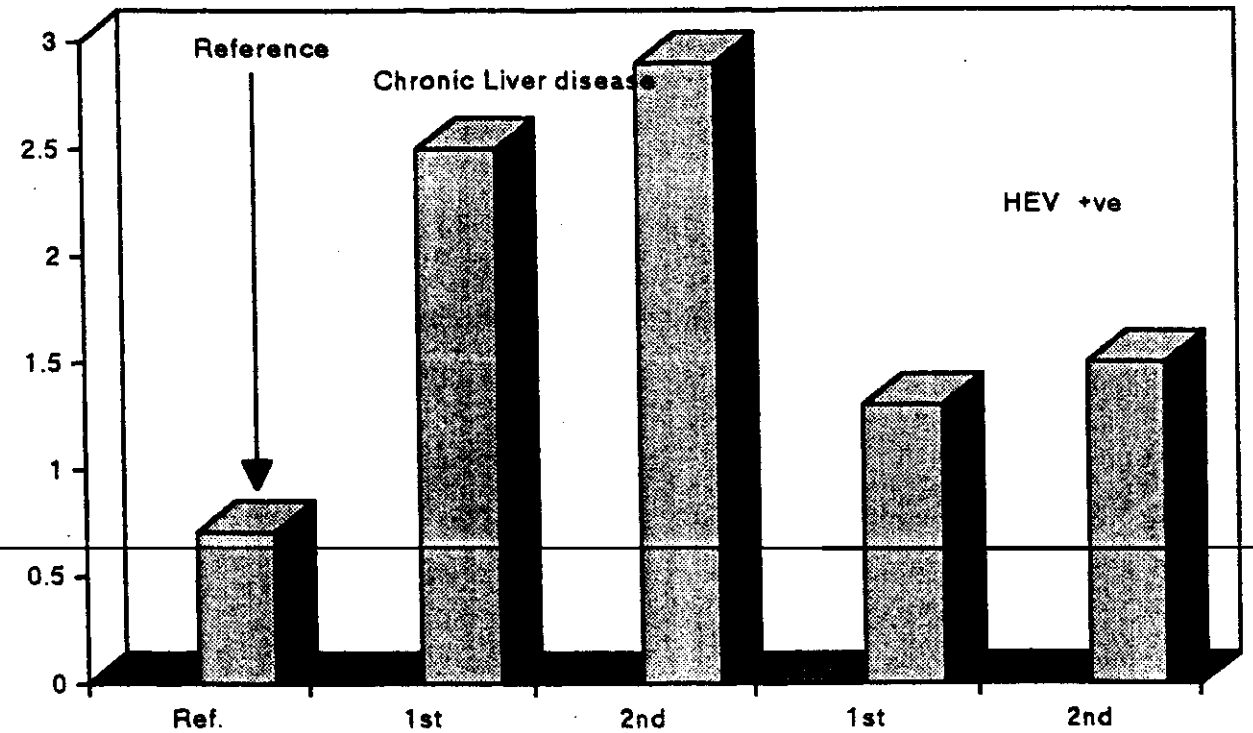

Figure (19): Total serum bilirubin in the reference group, first and second samples of chronic liver disease and hepatitis E virus +ve groups.

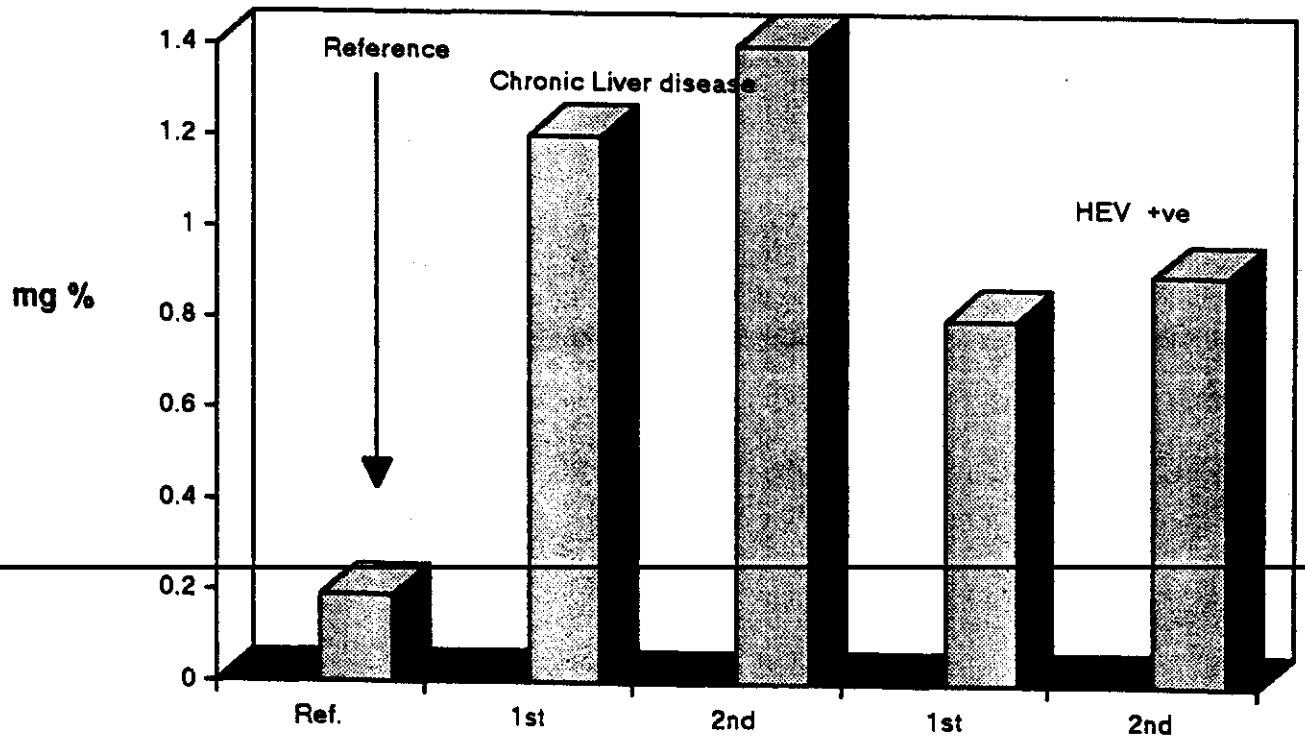

Figure (20): Serum direct bilirubin in the reference group, first and second samples of chronic liver disease and hepatitis E virus +ve groups.

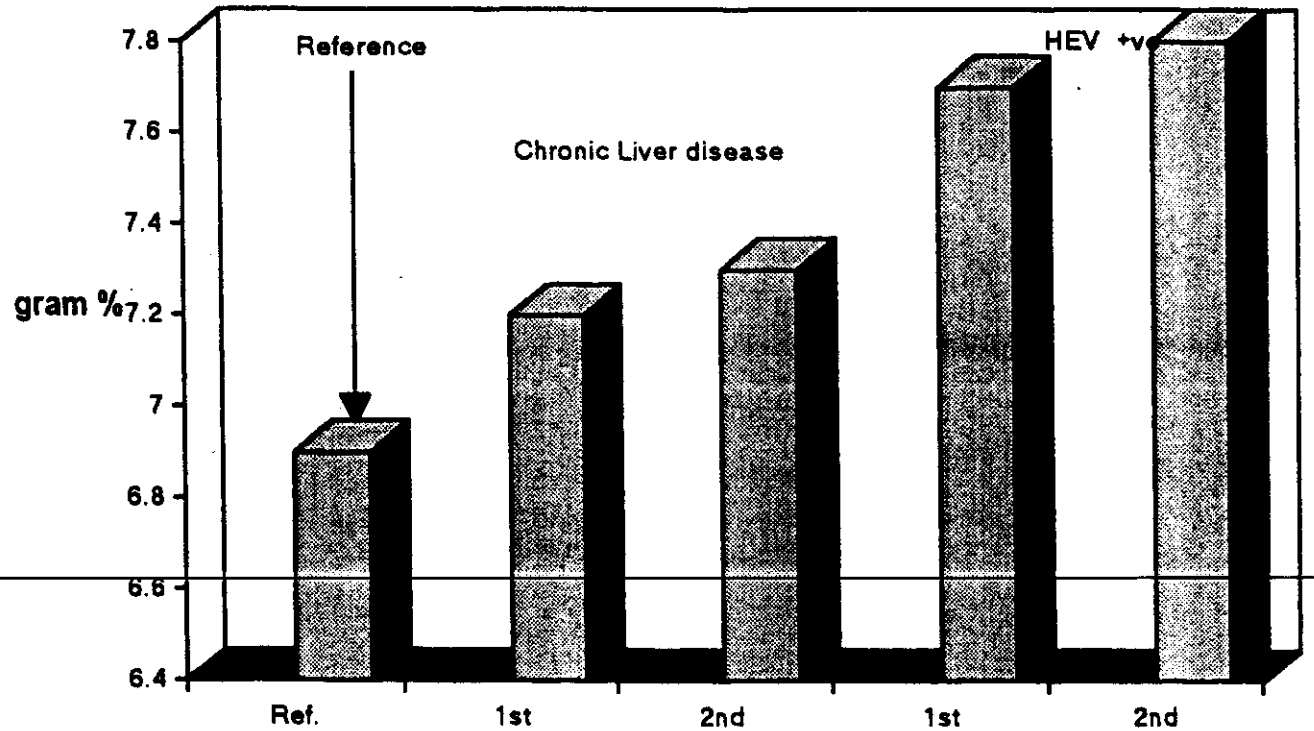

Figure (21): Total serum protein in the reference group, first and second samples of chronic liver disease and hepatitis E virus +ve groups.

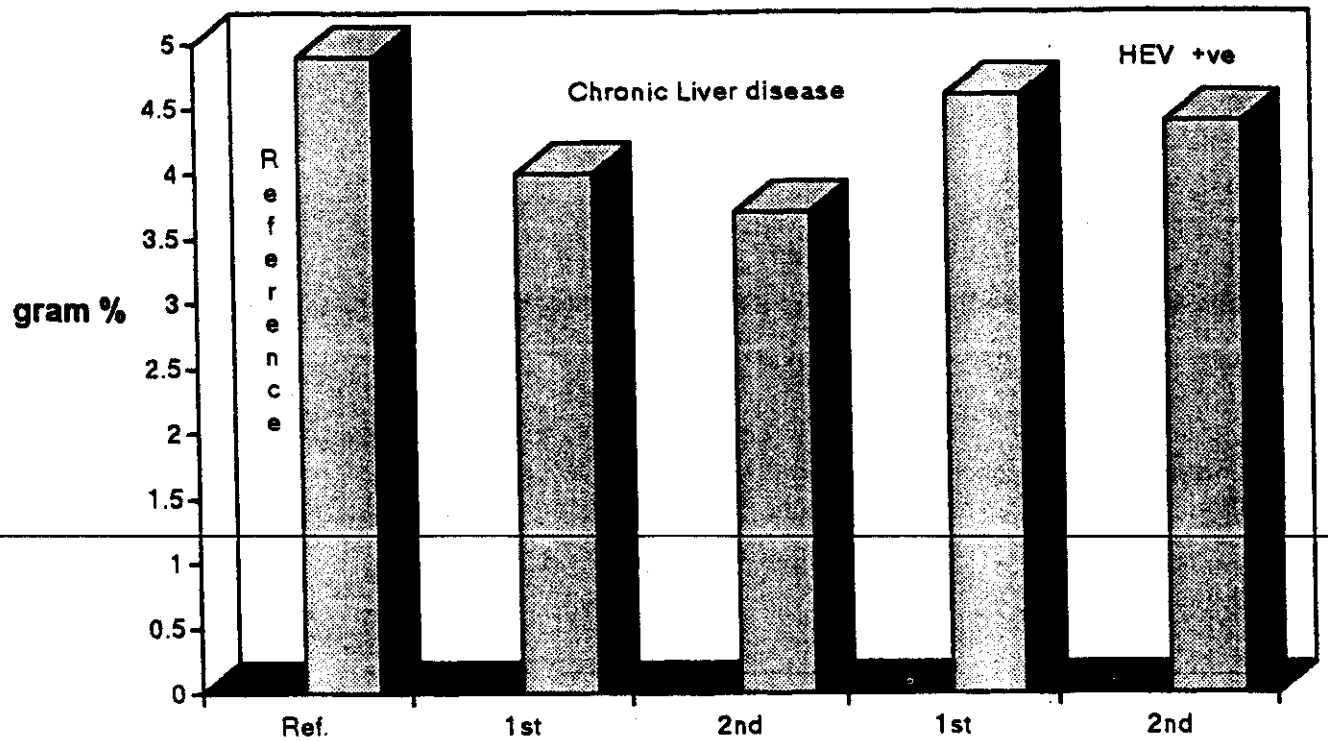

Figure (22): Serum albumin in the reference group, first and second samples of chronic liver disease and hepatitis E virus +ve groups.

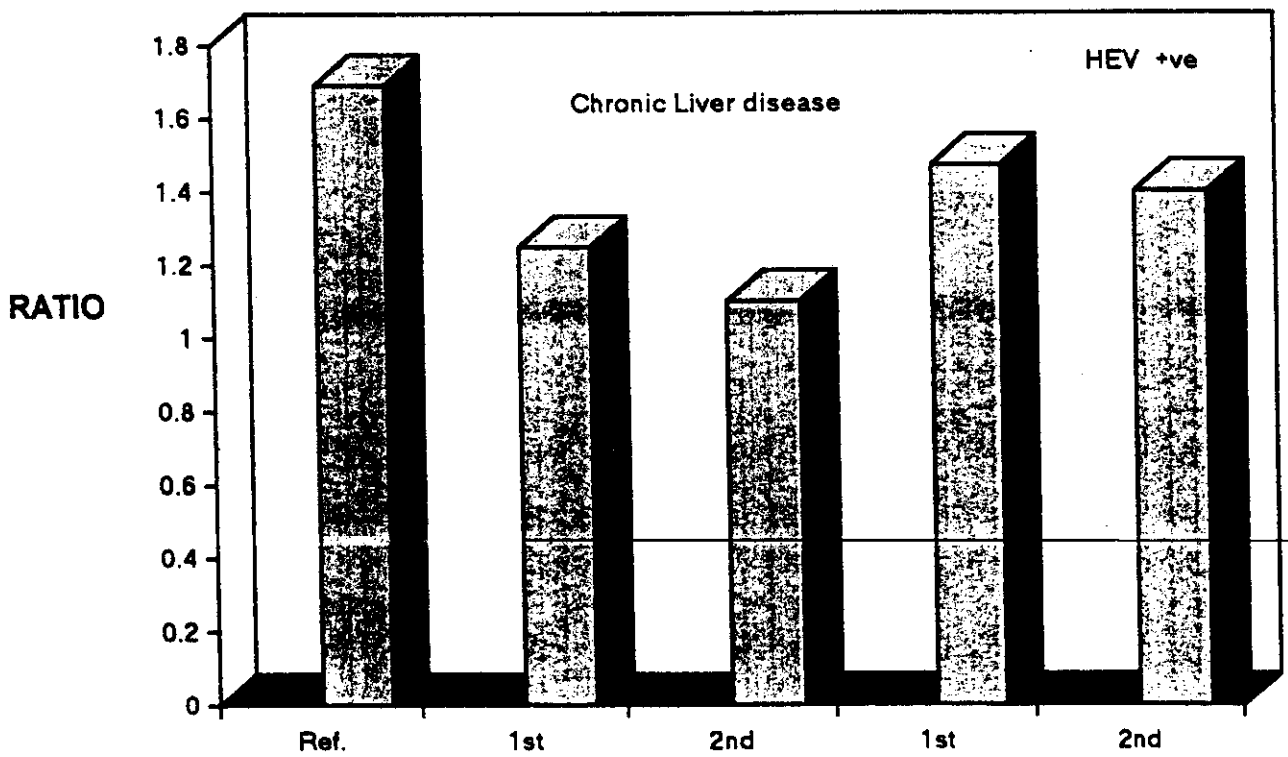

Figure (23): A/G ratio in the reference group,first and second samples of chronic liver disease and hepatitis E virus +ve groups.

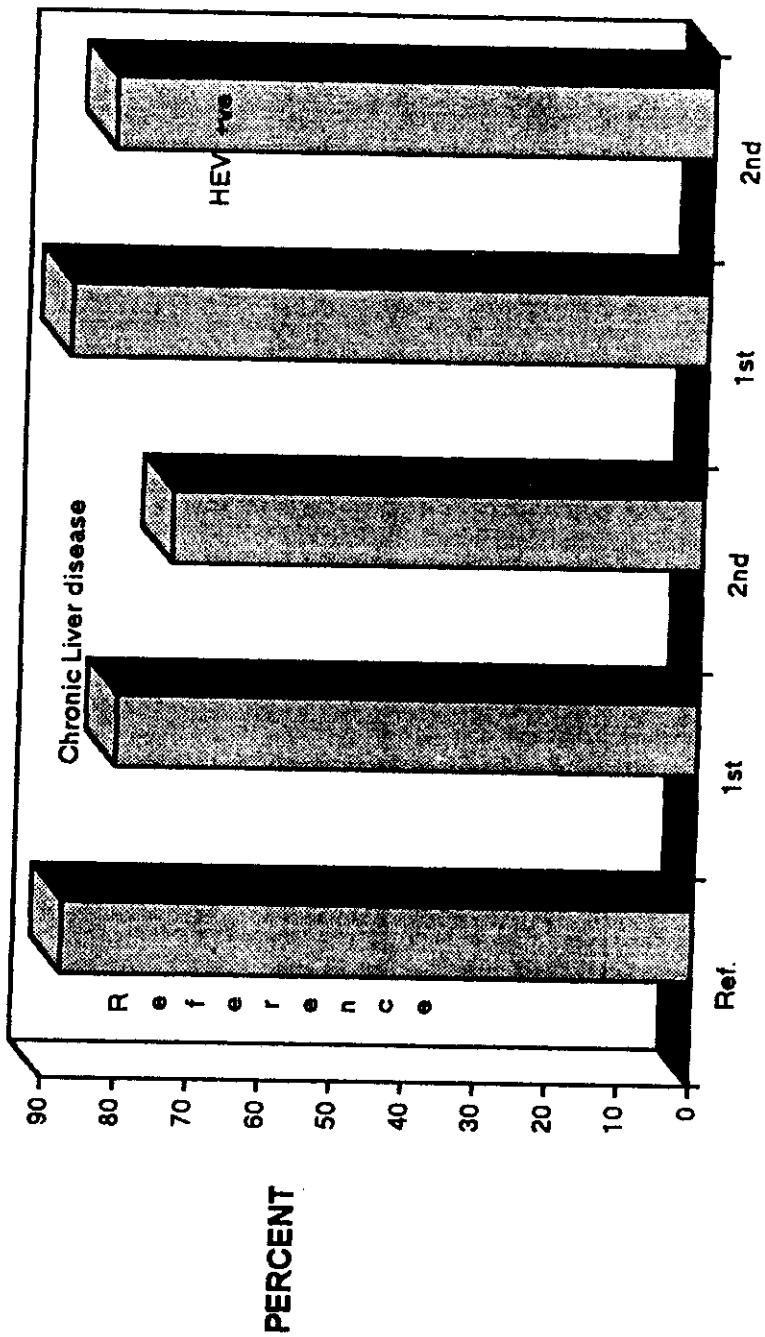

Figure (25): Prothrombin concentration in the reference group, first and second samples of chronic liver disease and hepatitis E virus +ve groups.

Table (27): The different cut off levels of serum TNF-alpha and the corresponding specificity and sensitivity values of each cut off level.

Cut off level (Pg/ml)	Specificity %	Sensitivity %
100	14.29	100
150	57.14	75
188.8	71.4	75
200	78.6	75
230	85.71	68.75
250	92.86	56.25
290	100	25

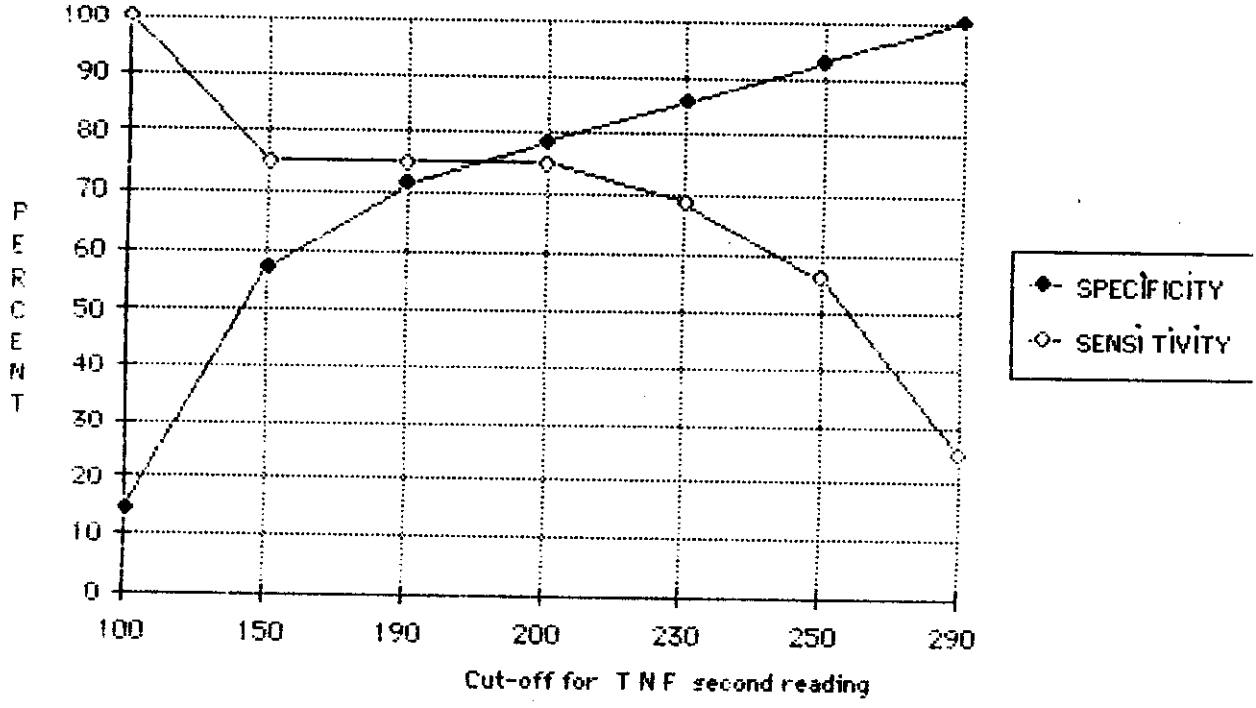

Figure (26): The different cut off levels of serum TNF-α and the corresponding specificity and sensitivity values of each cut off level.