

## Evaluation of Zinc Status in Patients with Liver Cirrhosis

Mohamed Shabaan<sup>1</sup>, Sayed Ibrahim El-Shayeb<sup>1</sup>, Mona Salah El-Dien<sup>1</sup>, Ayman Salah Abdellfattah<sup>2</sup>

<sup>1</sup> Internal Medicine, Faculty of Medicine, Menoufia University, Egypt.

<sup>2</sup> Ministry of Health, Egypt.

[dr\\_ayman424@yahoo.com](mailto:dr_ayman424@yahoo.com)

**Abstract: Objective:** The goal of our work is to evaluate zinc status in cirrhotic patients that may indicate the pathophysiological as well as therapeutic role of zinc in liver cirrhosis. **Background:** Cirrhosis is the development of regenerative nodules in response to chronic liver injury, which leads to portal hypertension and end-stage liver disease. Zinc (Zn) is an important unique salt with various effects that depends on catalytic and structural function in anvarious number of enzymes and “Zn-finger” proteins. Patients with cirrhotic liver have low level of serum Zinc and their clinical condition improves with Zinc supplementation. **Subjects and Methods:** This study was carried on 53 patients with cirrhosis of the liver and 10 normal volunteers as control. They include 33males and 20 females, their ages ranged from 33 to 70 years. Patients taken from inpatients and outpatient gastroenterology clinic of Menoufia University Hospital. Blood samples were obtained and for all these samples complete blood assay (CBC), Complete liver parameters (AST, ALT, Prothrombin time (PT), GGT, Alkphosphatase, and total bilirubin), estimation of serum zinc levels, albumin level in serum and abdominal ultrasound were done. **Results:** Our study shows that in cirrhotic patients, there is low level of serum Zinc and shows also that Child C patients had lowest serum level of Zinc than Child B or A. Our study also shows low level of Hb, platelets, GGT and albumin in patients rather than control also there are increased level of RBCs, ALT, AST, PT, INR and bilirubin in patients rather than control. **Conclusion:** There is low zinc level in serum of patients with liver cirrhosis. As cirrhosis increases, level of serum Zinc decreases. Hb, platelets, GGT and albumin are low while RBCs, AST, ALT, PT, INR and bilirubin are higher in patients with liver cirrhosis than control.

[Mohamed Shabaan, Sayed Ibrahim El-Shayeb, Mona Salah El-Dien, Ayman Salah Abdellfattah. **Evaluation of Zinc Statusin Patients with Liver Cirrhosis.** *Stem Cell* 2017;8(1):47-54]. ISSN: 1945-4570 (print); ISSN: 1945-4732 (online). <http://www.sciencepub.net/stem>. 10. doi:[10.7537/marssci080117.10](https://doi.org/10.7537/marssci080117.10).

**Key words:** Zinc, Liver Cirrhosis, Child-Pugh score, Platelet, bilirubin, Albumin.

### 1. Introduction:

Cirrhosis is a hassle of many liver sicknesses characterized by way of extraordinary shape and liver function. The sicknesses that result in cirrhosis accomplish that because they injure and kill liver cells, after which the irritation and repair this is related to the dying liver cells causes scar tissue to shape. Many causesof cirrhosis including chemicals (such as alcohol, fats, and positive medicinal drugs), viruses, poisonous metals (together with iron and copper that collect inside the liver because of genetic sicknesses), and autoimmune liver disorder in which the frame's immune device assaults the liver [1].

A few sufferers with cirrhosis are completely asymptomatic and feature a reasonably ordinary life expectancy. Different individuals have a multitude of the most extreme clinical pictures of cease-level liver ailment and a confined threat for survival. Common clinical features can also stem from reduced hepatic synthetic feature (e.g., coagulopathy), portal hypertension (e.g., variceal bleeding), or decreased cleansing abilities of the liver (e.g., hepatic encephalopathy) [2].

Zinc is a co-issue in DNA and protein synthesis and cellular department. It's miles believed to be crucial in wound healing. Zinc is second to iron as the maximum ample hint detail in the frame. zinc isn't always stored in the body but the frame consists of 2 to 3 g of zinc (Zn), observed specifically in bones, enamel, hair, pores and skin, liver, muscle, leucocytes and testes. [3].

One 1/3 of the of zinc located in plasma is hooked up loosely to albumin and approximately two thirds is firmly bound to globulins. Meat, liver, cereal merchandise, peas, beans, eggs, and seafood (particularly oysters) are true sources of zinc. Zinc absorption from meals is about 20-40%. Absorption of zinc is higher from fish and meat but decrease from wholegrain bread and cereals (phytate content material impairs absorption). zinc is especially excreted from frame in faeces [4].

Top 5 signs and symptoms of zinc deficiency are:

Compromised immune gadget: zinc influences mobile activities. Zinc deficiency can reason decreased or weakened antibodies and compromise the immune system. As a consequence the deficient person might be susceptible to infection or flu.

Diarrhea: a compromised immune gadget makes one vulnerable to infection. Any such infections are bacteria that reasons diarrhea.

Hair loss and pores and skin lesions: zinc is vital for normal cellular boom. Zinc vitamins deficiency weakens the cells, that may bring about hair loss in case of cells on the scalp and lesions on the pores and skin. That is one of the prominent signs of zinc deficiency.

Lack of appetite and/or anorexia: a deficiency of zinc causes lack of urge for food. If zinc deficiency isn't identified and dealt with, loss of appetite can ultimately result in anorexia.

Impairment of cognitive and motor capabilities: zinc deficiency in a pregnant mother cannot most effective weaken the mother, but also can motive damage to the fetus's neurological device, impairing the motor abilities and cognitive skills of the toddler [5].

Symptoms of acute zinc deficiency (anorexia, dysfunction of smell and taste, intellectual and cerebellar disturbances) and continual zinc deficiency (increase retardation, anemia, testicular atrophy and impaired wound recuperation) are not unusual in cirrhosis patients. it stays unresolved whether or not those low serum zinc concentrations in these disease states are indicative of genuine symptomatic or asymptomatic zinc deficiency, or simply replicate a lower in to be had zinc binding proteins [6], as properly over 90% of serum zinc is certain to protein in ordinary subjects [7].

A number of the scientific features of liver cirrhosis had been linked to zinc deficiency, including lack of body hair, testicular atrophy, bad appetite, immune dysfunction, altered taste and scent, reduced diet a and thyroid hormone metabolism, altered protein metabolism, behind schedule wound restoration and decreased drug elimination capacity[8]. one of the most interesting and novel components is the function of zinc deficiency in producing liver cirrhosis is the viable dating of zinc and hepatic encephalopathy (intellectual and cerebellar disturbances). Zinc is accountable for the activation of at the least 200 metalloenzymes. [9].

## 2. Subjects and methods:

This potential case control examine took six months (August 2015 until February 2016) this look at became carried on 53 patients with liver cirrhosis and 10 everyday volunteers as manipulate. They consist of 33males and 20 ladies, their age ranged from 33 to 70 years. Sufferers were decided on from inpatients and outpatient hepatology hospital of Menoufia college clinic. they were classified into 14 affected person of infant a, 25 affected person of baby b and 14 patient of child c. analysis of liver cirrhosis became completed

by using scientific, laboratory and radiological standards.

Inclusion standards:

Cirrhotic patients are included in our study and were categorized into A, B and C according to Child Pugh type.

Exclusion standards:

Cirrhotic sufferers related to concomitant sickness are excluded from look at like DM, HTN, and renal sicknesses. Seriously ill and disabled uncooperative sufferers are excluded from the study. Cirrhotic patients are categorized into A, B and C consistent with ChildPugh classification. All sufferers have been enrolled from August 2015 till February 2016 and gave oral consent to take part within the observe (by means of family of the affected person) which become accepted through the investigations and ethics committee of the college.

### All sufferers and controls are subjected to:

Records were taken together with age, sex, career and residence. Additionally past records of hepatitis, schistosomiasis and alcohol intake was taken.

Entire scientific examination along with chest, heart, abdomen and neurological examination.

Belly ultrasound to become aware of liver cirrhosis, presence or absence of splenomegally, presence or absence of ascites and presence or absence of focal lesions of liver.

Complete blood photo: complete blood relies changed into measured with penta-80 computerized blood counter [10].

Liver feature checks: willpower of AST, ALT, GGT, Alk phosphatase, general and direct bilirubin and serum albumin the usage of the Beckman coulter (SynchronCX nine ALX) medical autoanalyser, USA dedication of prothrombin time and concentration the usage of the fibrin timer 2 device of behring, Germany using sysmex okay-21, Japan [11 ].

Serum zinc stage: The measurements of serum zinc level become completed as observe: 2ml of blood became accumulated in citrated tube and centrifuged then serum turned into used.

Principle: Zinc present in the pattern is chelated by using zincon (2-carboxy-2-hydroxy-five-sulfoformazyl -benzene) within the reagent at alkaline ph. the formation of this complicated is measured at wavelength of 610 nm.

Pattern: serum, heparin plasma, CSF and urine. EDTA cannot be used.

### Regular values:

Serum or heparin plasma: sixteen-25micro mol per muddle (109-167micro gram in keeping with dl).

Urine: 69-25micro mol according to day (451+or-a hundred sixty five micro gram according to day).

Its miles endorsed that every laboratory must assign its very own normal variety as this is established upon geographical place.

Balance: when reagents stored at 4 °c, these would be stable up to the expiry date [12 ].

**Belly ultrasound:** it became achieved for all sufferers after fasting 8-12 hours to assist the prognosis of cirrhosis and to confirm ascitis and focal lesions if present or not. it becomes performed by using acuson/128x p/10 the use of pulsed array three.5 megahertz probe [13].

### Statistical analysis

Facts have been amassed, tabulated, statistically analyzed the usage of a personal laptop with statistical package deal of social science (SPSS) model 20, where the subsequent information were carried out.

Two varieties were executed from records:

Descriptive records: e.g. variety (no), percent (%), imply ( $\bar{x}$ ) and popular deviation (SD).

Analytic data: used to discover the possible association between studied factors and the centered sickness.

The used exams of importance protected:

Chi-squared test ( $\chi^2$ ): a parametric test used to find affiliation between two or greater qualitative variables [14].

Student t- test: is massively used test for contrast among two businesses having quantitative variables and with independent parametric information.

Mann-whitney check: is a check of significant used for evaluation between two organizations having quantitative variables with independent non-parametric records.

Kruskalwails check: for comparison among greater than two groups having quantitative variables and with independent non- parametric information.

One way ANOVA test: for comparison among greater than groups having quantitative variables and with independent parametric statistics.

Roc –curve: is a graph which is a receiver working feature curve. it's miles a plot of the real advantageous price against the false wonderful rate for the specific feasible cutoff-factors of a diagnostic test or marker [15 ].

Pearson correlation: is used to have a look at the correlation among usually distributed quantitative variables [16].

### 3. Results:

Zinc level is tremendous lower in affected person than control ( $p=0.001$ ). (Table1)

Zinc degree is significantly decrease in toddler C than A ( $p=0.03$ )but no big variations among A and B and between B and C. (Table 2)

**Table (1): Comparison between patient and control group regarding Zinc level:**

		Patient Group (No=50)	Control Group (No=10)	t- Test	P value
Zinc ( $\mu\text{g}/\text{dl}$ )	Rang	36-150	142-147	15.6	<0.001**
	Mean $\pm$ SD	83.49 $\pm$ 27.4	147.4 $\pm$ 5		

\*\*Highly significant difference

**Table (2): Comparison between patient groups (A, B, C) according to Child Pugh Score as regard Zinc level.**

Child Pugh Score	Zinc level		ANOVA	
	Range	Mean $\pm$ SD	F	P-value
A	50-150	97.74 $\pm$ 36.62	3.30	0.04
B	47-122	81.64 $\pm$ 20.4		
C	36-115	72.50 $\pm$ 23.44		
TUEY'S Test				
A & B	A & C		B & C	
0.16	0.03*		0.55	

\*Significant difference.

RBCs are significant higher in control than affected person ( $p=0.001$ ) also Hb is considerably lower in affected person than control ( $p =\text{zero}.001$ ) and also platelets are significantly lower in patient

than control ( $p =0.001$ ) however there were no big difference among affected person and control as WBCs. (Table 3)

There is no significant correlation between zinc level and liver function tests in patient groups (C) according to Child Pugh Score except ALP where there positive correlation between zinc level and ALP in cirrhotic patient in group C. (Table 4)

There's no widespread correlation between zinc degree and liver feature assessments in patient companies (B) in step with ChildPugh score. (Table 5)

There may be no considerable correlation between zinc level and liver characteristic assessments

in patient groups (A) in line with Child Pugh score. (Table 6)

There may be no tremendous correlation among zinc degree and ALT and AST in cirrhotic affected person additionally there's no big correlation between zinc level and ALP, GGT, PT and INR in cirrhotic patient and also there is no considerable correlation among zinc level and albumin and bilirubin in cirrhotic patient. (Table 7)

**Table (3): Comparison between patient and control group regarding CBC.**

	Patient Group (No=53)	Control Group (No=10)	t-test	P value
	Mean $\pm$ SD	Mean $\pm$ SD		
RBCs	3.82 $\pm$ 0.79	4.99 $\pm$ 0.28	5.32	<0.001**
Hb	10.12 $\pm$ 2.1	14.4 $\pm$ 0.79	6.52	<0.001**
WBCs	7.21 $\pm$ 3.7	7.31 $\pm$ 2.2	0.07	0.93
Platelets	145. $\pm$ 64.2	254.5 $\pm$ 74.9	4.81	<0.001**

\*Significant difference \*\*highly significant difference

**Table (4): Pearson correlation between serum level of zinc and liver parameters in patient groups (C) according to Child Pugh Score:**

Child Pugh Score	C	
	Zinc	
	R	P value
AST	-0.134	0.648
ALT	-0.30	0.920
ALP	0.516	0.059*
GGT	0.148	0.613
Albumin	0.131	0.655
Bilirubin	-0.236	0.416

**Table (5): Pearson correlation between serum level of zinc and liver parameters in patient groups (B) according to Child Pugh Score:**

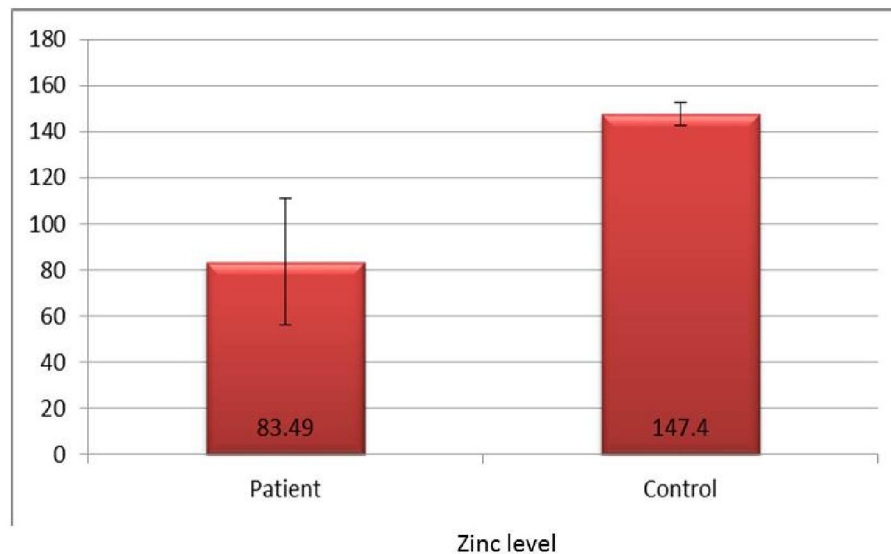
Child Pugh Score	B	
	Zinc	
	R	P value
AST	0.074	0.724
ALT	0.037	0.862
ALP	0.363	0.074
GGT	0.227	0.275
Albumin	0.096	0.649
Bilirubin	-0.167	0.424

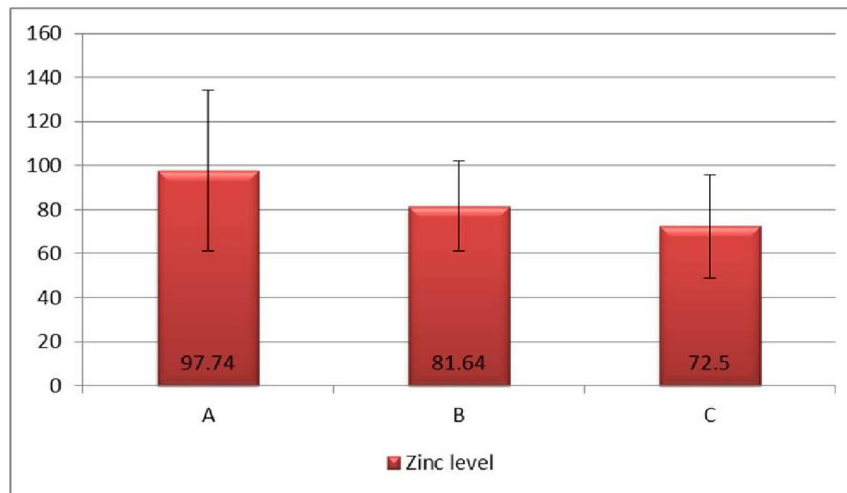
**Table (6):** Pearson correlation between serum level of zinc and liver parameters in patient groups (A) according to Child Pugh Score:

Child Pugh Score	A	
	Zinc	
	R	P value
AST	-0.095	0.746
ALT	0.039	0.894
ALP	-0.009	0.977
GGT	-0.265	0.360
Albumin	-0.111	0.707
Bilirubin	-0.025	0.932

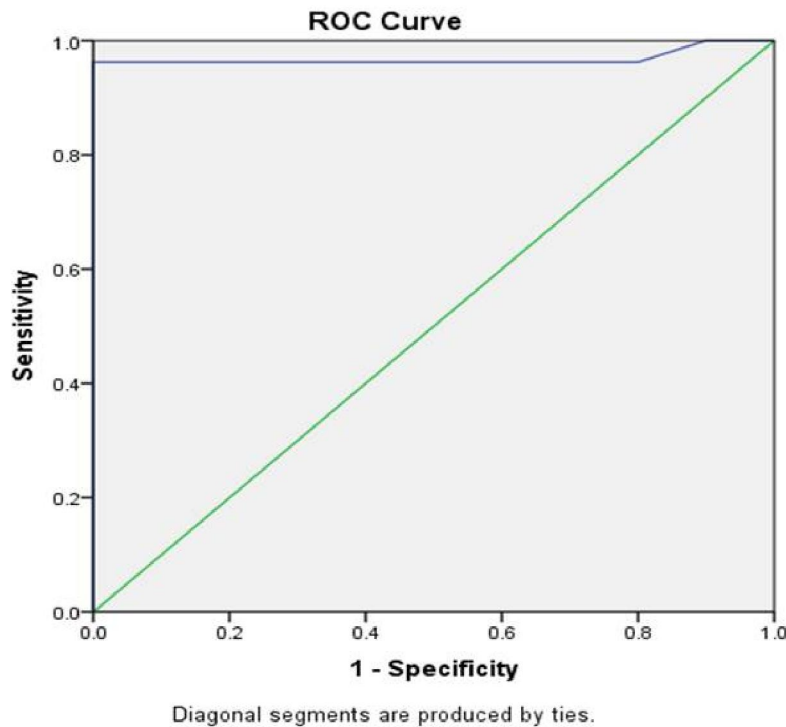
**Table (7):** Pearson correlation between serum level of zinc and other parameters in cirrhotic patient:

	Zinc	
	r	P value
AST	-0.032	0.82
ALT	0.075	0.591
ALP	0.242	0.080
GGT	0.052	0.713
PT	-0.0198	0.156
INR	0.105	0.455
Albumin	0.050	0.724
Bilirubin	-0.210	0.09

**Figure 1:** Contrast between affected person and subjects who are control regarding zinc level.



**Figure 2:** Assessment between affected person agencies (A, B, C) in step with Child Pugh score as regard Zinc level.



**Figure 3:** ROC curve of serum Zinc in affected person with liver cirrhosis.

#### 4. Discussion:

Cirrhosis is a slowly progressing disease in which wholesome liver tissue is replaced with scar tissue, finally saving the liver from functioning nicely. The scar tissue blocks the drift of blood through the liver and slows the processing of nutrients, hormones, drugs, and evidently fashioned pollution. it additionally slows the production of proteins and other substances made with the aid of the liver through **Conn & Atterbury** [17 ]..

Zinc is vital element. It is responsible for various physiological roles. Zinc is most critical for the tissue growth and repair. Zinc is having specific position in the function of the 300 enzymes. It has defensive role against the fibrosis. Zinc prevents the cell harm specifically resulting from the oxidative stress. [18]. The non-vegetarian food has rich quantity of zinc. The organ meat contains the highest attention of Zinc. Inside the globe over 2 million peoples are having Zinc deficiency. Hence the zinc dietary supplements

are given to conquer the deficiency. There is a term responsible for many side effects. These side effects include slow wound healing. In children side effects includes undersized growth and acute diarrhea by **Khan**[19].

In our examine, there was no significant difference between patients and control group concerning age and gender. 43.5% of our sufferers had ascitis, 52.8% with lower limb edema, and 32.1% has splenomegally and 62.2% of jaundice as concerning clinical information.

As regard etiology of our cirrhotic patients, twenty nine of them had been post hepatitis C cirrhosis, five of them post bilharziasis, seven of them post hepatitis B cirrhosis, three of them were alcoholics, five of them had been autoimmune & four were NASH.

We showed vast difference among cirrhotic subgroups A, B & C regarding liver functions exams particularly ALT, AST, bilirubin & PT which eminent among Child A & C and between Child B & C cirrhosis.

Inside our study, a widespread difference between cirrhotic subgroups concerning serum zinc level especially between subgroup A & C. The equal finding pronounced by means of **Mohammad et al.** [20] and located that serum zinc level was extra correlated with level of liver fibrosis and added that supplementation of Zinc to cirrhotic sufferers may gradual the progression of liver fibrosis and restrain the improvement of liver carcinogenesis. The identical findings reported by using **Takagii & Yoshida** [21], observed that the blood zinc concentrations decreases with development of the disorder from chronic hepatitis to compensated liver cirrhosis and to decompensated liver cirrhosis and to hepatocellular carcinoma moreover **Grungriff**, [22] and **Marshenseni**, [23] showed that sufferers with liver cell failure or HCC are in an especially severe nation of zinc deficiency and liver damage is located to be repaired with zinc supplementation.

In the present study, a sizeable distinction became obvious among our cirrhotic patients and normal control groups regarding Hb%, RBCs, WBCs & platelet within the addition to giant distinction regarding to AST, ALT which revealed by **Shunichi, et al.**, [24]. and discovered a tremendous lower in liver enzymes after Zinc supplementation.

Also in our study, serum zinc stage drastically lower in our cirrhotic patients than wholesome control groups which can also expect the condition among the progression of liver harm and zinc deficiency and how the cirrhotic patients might also get benefit from zinc supplementation which suggested via **Cabre & Camps** [25].

### Conclusion:

This examine found that zinc stage in serum of sufferers with decompensated cirrhotic liver and this is discovered in also many studies. This examine showed that a sizeable distinction among zinc stage as cirrhosis degree expanded that hypozincemia is extra outstanding. This observe additionally showed no huge correlation between zinc degree in patients serum and liver enzymes (AST, ALT & GGT) however albumin stage is associated with zinc level in cirrhotic sufferers as decreased albumin level correlate decreased zinc degree.

### References:

1. Dennis Lee and Jay W, Liver cirrhosis, Causes, Symptoms, Diagnosis, and Treatment.
2. Sherlock S and Dooley J editors, Liver problems and Biliary System. 11th Edition. Blackwell Science; Oxford, UK; Malden, MA.
3. Shrimpton R, Gross R and Darnton-Hill I, Deficiency of Zinc: what are the most common interventions? BMJ.
4. Eastwood M, in Oxford Textbook of Medicine 3rd Ed OUP.
5. Prasad AS, Deficiency of Zinc in humans: a neglected problem. J Am Coll Nutr.
6. Riggio O., Merli M., Capocaccia L., Caschera M., Zullo A., Pinto G., Zinc intake reduce blood level of ammonia and increases ornithintranscarbamirase in liver activity in experimental cirrhosis. Hepatology. 1992; 16: 785-789.
7. Ray G and Ghoshal U.C, Aetiological spectrum of chronic liver disease in eastern India. Trop Gastroenterol. 21(2): 60-62.
8. Boyett J.D., Sullivan J.F. Distribution of Zinc protein-bound in healthy people and cirrhotic serum. Metabolism. 1970;19:148-157.
9. Misra B and Panda C, Study on knowledge about hepatitis B viral infection in coastal eastern India. Int J Hep B Annual. 6(1): 19-28.
10. Stoll BJ: Infections of the Neonatal Infant. Nelson Textbook of Pediatrics, 18th ed. Elsevier 2008; 109: 794-811.
11. Conradie JD and Mbhele BE, South African Medical Journal, vol. /is. 58/4(169-71), 0256-9574.
12. Serrao, MRI with hyperpolarised [1-13C] pyruvate detects advanced pancreatic preneoplasia prior to invasive disease in a mouse model. Gut 65:465-75 (2016).
13. Hayakawa R, Jab J, Toxic environ, Health 8, 14-18(1961).
14. Chen L. Abdominal ultrasound imaging. In: Sahani DV, Samir AE, eds. Abdominal Imaging. 2nd ed. Philadelphia, PA: Elsevier; 2017: chap 3.

15. Ryabko B. Ya, Stognienko V.S and Shokin Yu. I. "A new test in application to some cryptographic problems", *Journal of Statistical Planning and Inference*. 123: 365–376. Retrieved 18 February 2015.
16. Powers and David MW, "ROC-Con Cert: ROC-Based Measurement of Consistency and Certainty". *Spring Congress on Engineering and Technology (SCET)*. pp. 238—241.
17. Hotelling, H. "New recent Correlation Coefficient and its New Transforms". *Journal of the Royal Statistical Society. Series B (Methodological)*. 15 (2): 193–232.
18. Conn H & Atterbury C, Cirrhosis. In, Schiff L, Schiff E, editors. *Diseases of the Liver*. 7th edition. Lippencott Company, Philadelphia, 875-934.
19. Arakawa Y., Tanaka N, Moriyama M., *Hepatic Problems and Trace Elements*. Gatsukaijimu center; Osaka, Japan,; 2003. pp. 1–30. (In Japanese).
20. Kahn AM, Helwig HL and Redeker AG, Urine and serum zinc abnormalities in disease of the liver. *Am J Clin Pathol*. 1965;44:426-435.
21. Mohammad MK, Zhou Z and Cave M, *Nutr Clin Pract*. 27(1):8-20. doi: 10.1177/0884533611433534. Review. Erratum in: *Nutr Clin Pract*.27(2):305.
22. Takagii and Yoshida, Role of Zinc deficiency/Zinc supplementation on metabolism of ammonia in patients with end-stage liver cirrhosis. *Acta Med Okayama*, 55, 349- 355.
23. Grungreiff, Liver cirrhosis and "liver" diabetes mellitus are linked by Zinc deficiency. *Med Hypotheses*, 64,316-317.
24. Marchesini, Zinc administration and metabolism of amino acid-nitrogen in patients with end-stage liver cirrhosis. *Hepatology*, 23,108492.
25. Shunichi Matsuoka, Hiroshi Matsumura, Hitomi Nakamura, Shu Oshiro, Yasuo Arakawa, Junpei Hayashi, Zinc intake reduce serum blood level of ammonia and increases ornithintrans carbamirase of the liver activity in experimental cirrhosis. *Hepatology*. 1992;16:785–789.
26. Cabre M and Camps J The role of Zinc as an antioxidant and also hepatoprotective are related to cytochrome P450 suppression and metallothionein promotion in rats with experimental cirrhosis. *Int J Vitam Nutr Res.*, 71,229-236.

3/21/2017