

Evaluation of Sorbitol Dehydrogenase and Some Biochemical Parameters in Patients with Hepatitis.

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Abstract

This research was concerned with a study of the relationship between sorbitol dehydrogenase and hepatitis disease . Blood samples have been drawn from (35) patients with hepatitis and (28) blood samples of healthy as control group ages ranges from (40-65) years. Patients were collected from Al-Salam Hospital in Mosul City under the supervision of specialists Live in Mosul city. Sorbitol dehydrogenase, total serum bilirubin, protein, albumin, globulin and alanine aminotransferase sGPT were measured in blood of these patients. The results showed a significant increase in sorbitol dehydrogenase, sGPT, bilirubin, total serum protein, albumin and globulin levels compared with the control group. There was also study of the relationship between (SDH) activity and the studied parameters in patient group and finding that there are liner correlation coefficient. the results indicated that, there was a positive significant correlation between the activity of enzyme and each of the total protein, albumin, globulin, sGPT, and bilirubin and negative significant corolation between SDH and globulin.

Keywords: Sorbitol dehydrogenase, hepatitis, sGPT.

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تقدير مستوى انزيم السوربيتول ديهيدروجينيز وبعض المتغيرات الكيموحيوية في مرضى التهاب الكبد

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المخلص

اهتم هذا البحث بدراسة العلاقة بين انزيم السوربيتول ديهيدروجينيز ومرض التهاب الكبد. تم أخذ عينات دم من (35) مريض مصاب بالتهاب الكبد و (28) عينة دم كمجموعة ضابطة تتراوح أعمارهم بين (40-65) سنة، تم جمع عينات المرضى من مستشفى السلام بمدينة الموصل وبإشراف أطباء اختصاص ويعيشون في مدينة الموصل. تم قياس انزيم السوربيتول ديهيدروجينيز، البيليروبين الكلي، البروتين، الألبومين، الكلوبولين والألانين أمينوترافاز SGPT في دم هؤلاء المرضى. أظهرت النتائج زيادة ملحوظة في انزيم السوربيتول ديهيدروجينيز و SGPT و البيليروبين مقارنة مع المجموعة الضابطة. في حين كان هناك زيادة في مستويات البروتين الكلي في المصل والألبومين والكلوبولين بشكل كبير عند المقارنة مع مجموعة الضابطة. وعند دراسة العلاقة الخطية من خلال ايجاد معامل الارتباط الخطي بين فعالية الانزيم والمتغيرات المقاسة في البحث كان هناك ارتباط إيجابي كبير بين نشاط الإنزيم وكل من البروتين الكلي، الألبومين، الجلوبيولين، SGPT، والبيليروبين في مجاميع المرضى.

الكلمات الدالة: انزيم السوربيتول ديهيدروجينيز، التهاب الكبد، كلوتاميت بايروفيت ثلاثي الفوسفات.

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1. Introduction:

The polyol pathway is a secondary pathway to metabolize glucose, and contains two enzymes from dehydrogenases, Aldose reductase (AR) (EC 1.1.1.21) and sorbitol dehydrogenase (SDH) (EC 1.1.1.14). The flow of the polyol pathway under normal conditions is low but SDH will increase in the case of serum blood glucose, the flow of the polyol pathway will increase. In other words, there is a rise in glycolysis from the normal level. This increase may lead to an intermediate accumulation Of sorbitol, which is unable to cross cell membranes. The large increase in the concentration of the polyol pathway can lead to osmotic imbalance, Of extracellular fluid inward causing cell bulge. See in Fig 1.

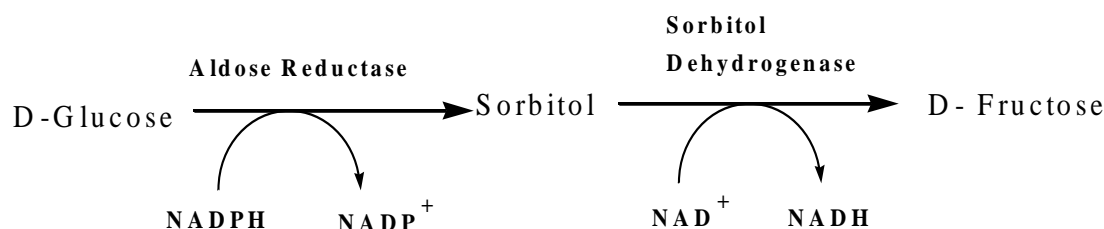


Fig. 1: The polyol metabolic pathway.

The most complex pattern of sorbitol dehydrogenase enzymes has been established for human liver [1]. Although sorbitol dehydrogenase is widespread in nature, is common in liver, and has been structurally characterized from several sources. Its exact function in mammalian organs generally has remained unclear. In addition to ethanol oxidation, function in bile acid formation, fatty acid degradation, vitamin A metabolism have been considered [2,3]. Another common liver enzyme sorbitol dehydrogenase, was shown to be structurally, mechanistically, and ancestrally related to alcohol dehydrogenase [4,5]. SDH or Sorbitol dehydrogenase is a cytosolic enzyme. In humans this protein is denoted by the SORD gene [6].

Carbohydrate metabolism of Sorbitol dehydrogenase is converting sorbitol. The sugar alcohol form of glucose, into fructose [7,8], together with aldose reductase, it provides a way for the body to produce fructose from glucose without using ATP. Sorbitol dehydrogenase uses NAD as a cofactor [9,10]. Organs that use it most frequently include the liver and seminal vesicle. It is found in all kinds of organisms from bacteria to human. [11] A secondary use is the metabolism of dietary sorbitol though it is known not to be absorbed as well in the

intestine as its related compounds glucose and fructose ,and is usually found in quite small amounts in the die (except when used as an artificial sweetener) [12].

The aim of this study was to evaluate the relationship between sorbitol dehydrogenase and some biochemical parameters in patients with hepatitis.

2. Materials and Methods:

Patients sample were collected from Al-Salam Hospital in Mosul City under the supervision of specialists live in Mosul city ages rangs from (40-65) years. Five milliliters of blood sample were collected from each patient and leave it for (15) minutes at room temperature for coagulation, then serum can be separated by centrifugation at (1075.2 x g) for (10) minutes. Serum was kept frozen at (-20C) until used [13]. Total serum protein (T.S.P.) was measured by Biuret method using kit manufactured by RANDOX (united kingdom). Serum albumin was measured by dye \pm binding method using kit manufactured by RANDOX (united kingdom). The concentration of serum globulin (Glb) was calculated for each person according to the following formula: C globulin= C total protein – C albumin

Where C (mg ldL) = concentration of serum globulin

Total protein and albumin , expressed in mg ldL [14]. Serum alanine amino transferase ALT(sGPT)was determined by an enzymatic method using a kit manufactured by bioMerieux (france) . Total serum bilirubin was determined by using a kit manufactured by biocon (Germany) . The activity of sorbitol dehydrogenase was estimated by the manual method [15].

Statistical analysis:

Data analysis were performed using SPSS software versin 10.0. Results were reported as mean \pm standard deviation .comparisons between patients and control group were carried out using the independent, samples T-test. A value of $P < 0.05$ indicates statistical significance.

3. Results and Discussion:

The results of different biochemical parameters were represented as(mean \pm SD) for patients and control group in [Table 1](#).

Table 1: level (mean \pm S.D) of biochemical parameters in all studied group.

Parameters	Mean \pm S.D.		P-value
	Patients	Control group	
S.D.H. U/ml	0.98 \pm 0.39	0.25 \pm 0.01	<0.001*
S.GPT mg/L	6.4.1 \pm 0.2	4.7 \pm 3.7	<0.0001*
T.S.B. mg/L	2.697 \pm 0.8	0.7 \pm 0.2	<0.001*
T.S.P. mg/dl	9.6 \pm 2.3	6.3 \pm 3.1	<0.0001*
S.Alb mg/dL	6.1 \pm 1.5	3.5 \pm 0.5	<0.01*
S.Glb mg/dL	3.5 \pm 0.7	2.8 \pm 1.2	<0.01*

*p<0.01 sig.

Enzyme U: The amount of the enzyme that converts one micro gram of substrate to one milliliter per min of serum.

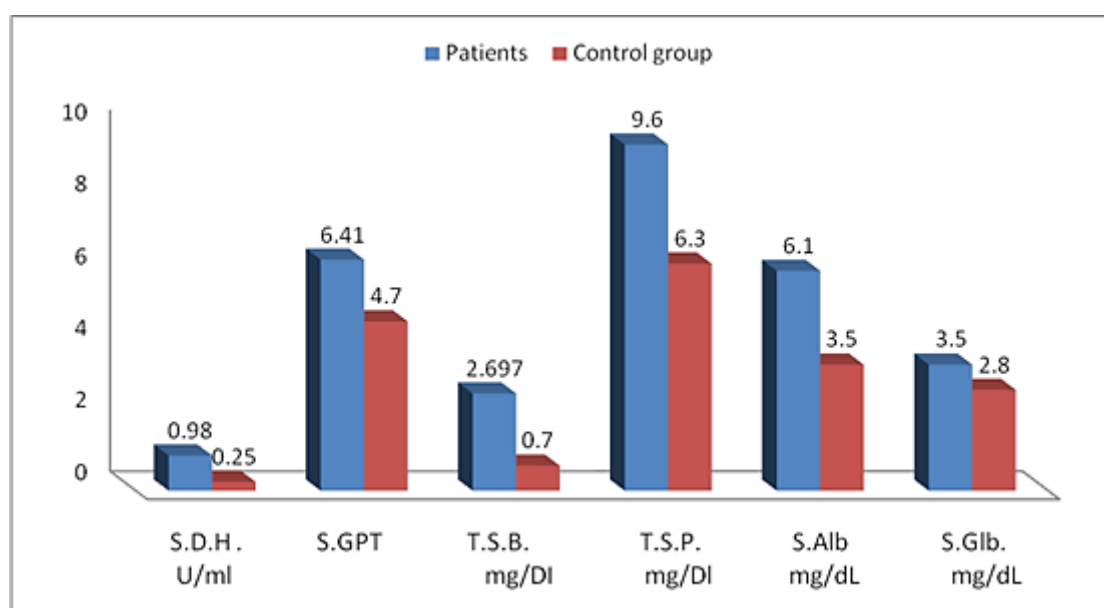


Fig. 2: comparison between the patients and control groups for all measured parameters.

From Table 1 the results indicated that there were a significant increase in SDH, sGPT, TSB, TSP, Alb and Glb in patients compared with the control group. similar results were arrived at by other investigators in SDH, sGPT, TSB, [16,17,18].

To find the relationship between the efficacy of SDH and the measured biochemical parameters in patients and control group. A correlation coefficient (r) was determined.

For patients group, there were a significant positive correlation (r) in the level of probability between the activity of SDH with total protein, albumin, globulin, SGPT and T.S.B, as shown in Figs. 1, 2, 3, 4, 5 respectively.

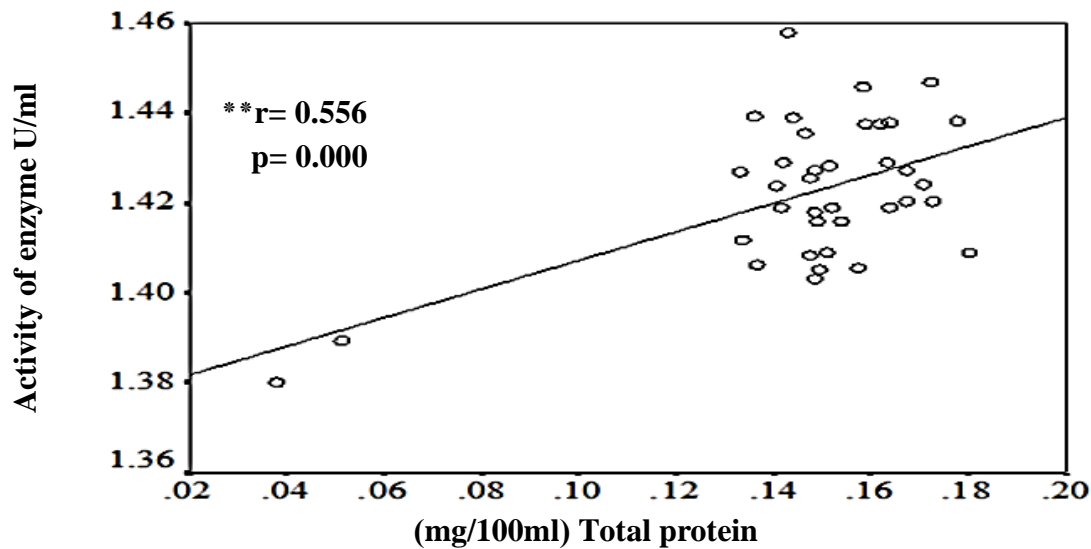


Fig. 3: the relationship between enzyme activity SDH and TSP level in serum patients group.

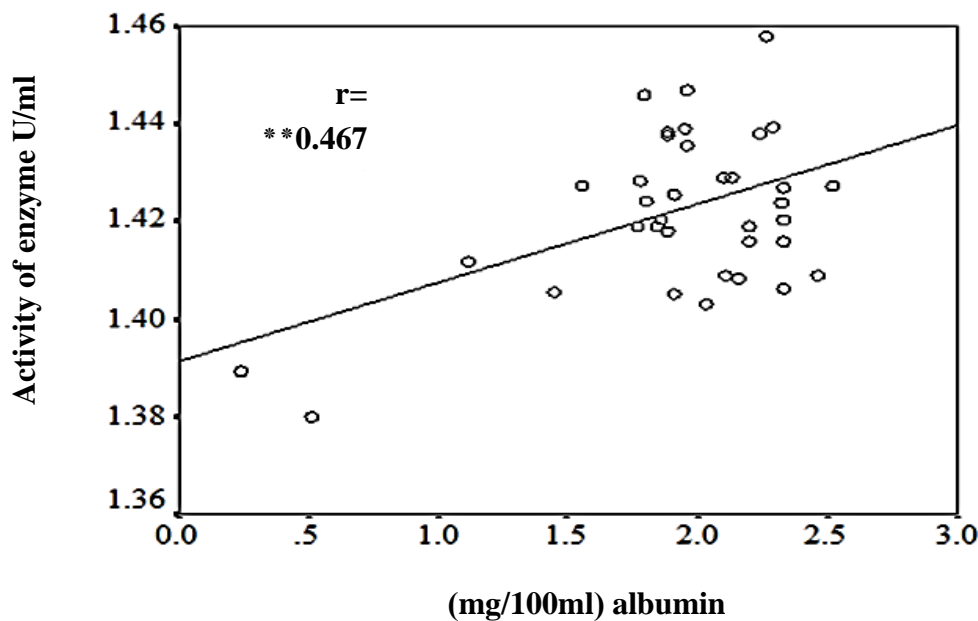


Fig. 4: the relationship between enzyme activity SDH and albumin level in serum patient group.

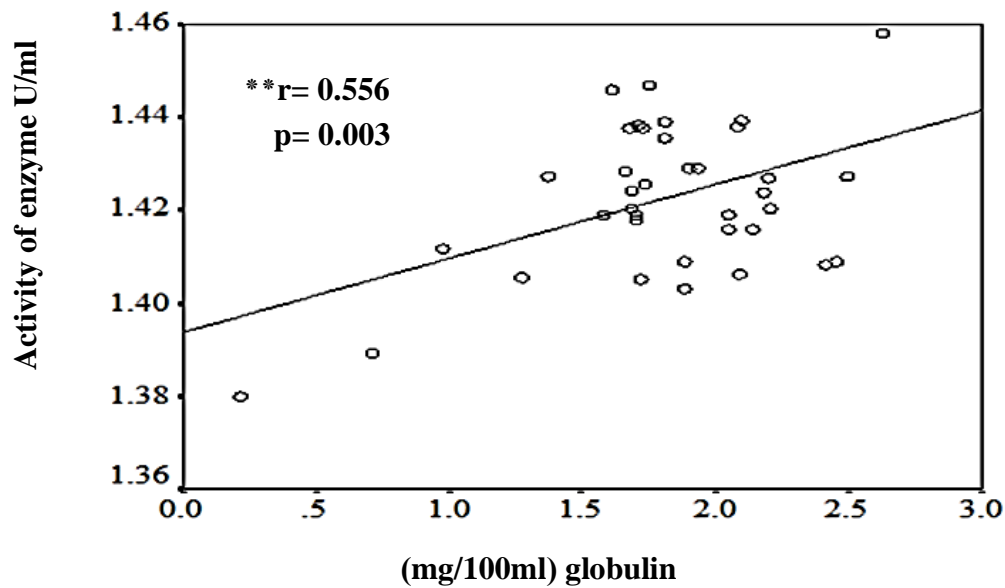


Fig. 5: the relationship between enzyme activity SDH and globulin level in serum patient group.

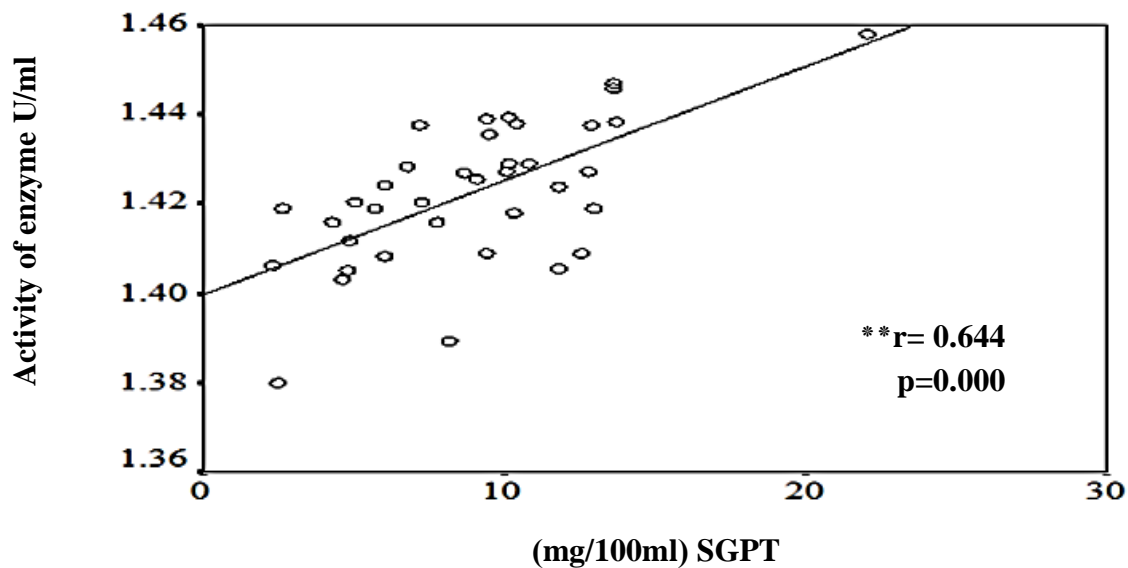


Fig. 6: the relationship between enzyme activity SDH and sGPT level in serum patient group.

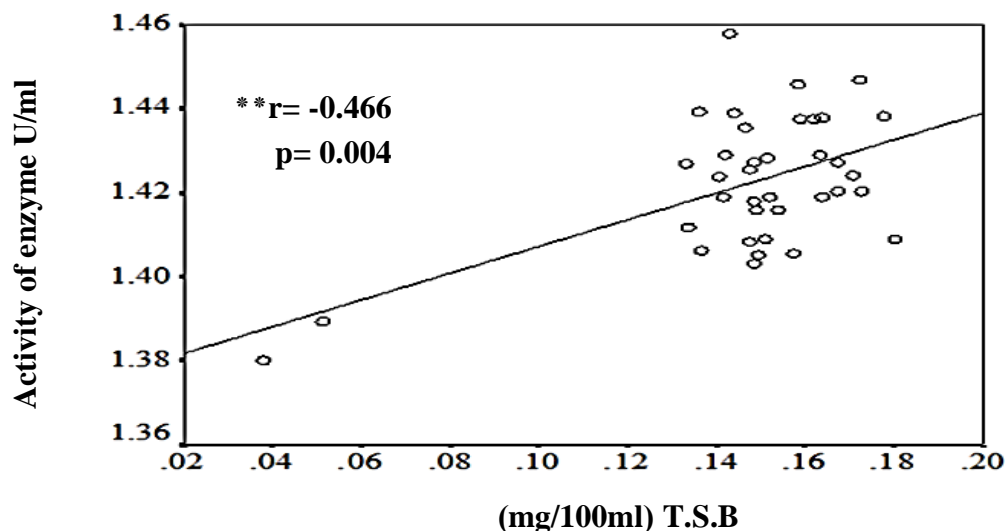


Fig. 7: the relationship between enzyme activity SDH and T.S.B level in serum patient group

These results are similar to those of researchers [23,24], who found the liver metabolic volume and liver functional are complementary to each other, The liver metabolic volume and blood flow determine its functions in most cases, which also depend on the relative ratio and the effect of interactive the two factors [13]. When liver fibrosis and portal hypertension occur, necrosis of liver cells, hyperplasia of fibrous tissue, formation of unreal lobules and abnormality of liver microcirculation will result in decrease of liver metabolic volume, increase of anatomical and physiological intra liver shunt and change of their .

The results obtained agree with the research [25,26] which was interested in the study the evaluation whole-body removal kinetics of sorbitol, the use of extrarenal sorbitol clearance to estimate hepatic plasma flow in humans, and to compare measurements of liver flow by Fick's principle [17].

Liver functional blood flow is a part of total liver blood flow that enters the liver sinusoid includes in the metabolic process [12]. actually it can only be determine by assay of its clearance rate. D-sorbitol is the first substance suitable for noninvasive evaluation of hepatic blood flow

The increase in the metabolism of glucose through the polyol pathway is probably the most important[17]. High blood sugar increases the rate of cellular juice (NADH / NAD) in the red blood cells. The value of the Michaelis-Menten constant (Km) (70 mM), the glucose

reduction rate for sorbitol will increase with increased levels of glucose in tissues that do not need insulin to absorb excess glucose [19].

Other studies have been pointed out Serum and liver sorbitol dehydrogenase (SDH) and glutamic-oxalacetic transaminase (GOT) activities were studied in rats after carbon tetrachloride (CCI4) injections. An inverse relationship was observed between the increased serum and decreased liver SDH activities. The extent of hyper enzymemia was proportional to the dose of CCI4. Outside of the skeletal muscle mass SDH was found predominantly in the liver of animals and humans autopsy material as a rule there is no detectable SDH activity in the liver of animals and humans autopsy material in the serum of patients who do not have liver disease or in normal volunteers. At the most they may have up to 3 units of activity per milliliter of serum. Elevated serum SDH activity has been detected in 26 of 30 determinations on 22 patients with acute viral hepatitis (87 per cent), in 21 of 48 studies with cirrhosis of the liver (44 per cent), and 3 of 8 patients with malignancy in the liver (37.5 per cent). (In 6 patients with extrahepatic obstruction there was no significant serum SDH activity detectable although the patients were markedly jaundiced and although several of the other serum enzymes studied, such as SGOT, SGPT, and SLDH, were elevated [20-22,27].

References

- [1] J. Holden, R. Yang, D .Pope. "*Hepatitis A immunisation in persons not previously exposed to hepatitis A*", Cochrane Database System Rev. 7: CD009051, (2012).
- [2] B. A. Connor "*Hepatitis A vaccine in the last-minute traveler*", American Journal Medicin, 118, 58 (2005).
- [3] CY., Zhang, Lu S, Ao YY, *et al.*, "*A novel hepatovirus identified in wild woodchuck Marmota himalayana*", Scientific Reports, 6, 22361,(2016).
- [4] J. Cristina, M. Costa-Mattioli, "*Genetic variability and molecular evolution of hepatitis A virus*", Virus Research. 127 (2), 7 (2007).

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- [5] C .Wheeler, Vogt TM, Armstrong GL, et al. "*An outbreak of hepatitis A*", Journal of Medical Virology, 66 (1), 7 (2005).
- [6] VS .Paula, ML. Baptista, E. Lampe, *et al.*, "*Characterization of hepatitis A virus isolates from subgenotypes IA and IB in Rio de Janeiro, Brazil*". Journal Medicin Virol. 66 (1): 7, (2002).
- [7] P. R. Murray, K. S. Rosenthal, & M. A. Pfaller,. "*Medical Microbiology*", 5th Ed., Elsevier Mosby (2005).
- [8] G .Molino, P. Avagnina, G. Belforte, J. Bircher, "*Assessment of the hepatic circulation in humans: new concepts based on evidence derived from a D-sorbitol clearance method*", Journal Labrotary Clinical Medicin, 131, 393 (1998).
- [9] N .Tygstrup, JO .Clemmesen, P. Ott. "*Hepatic plasma flow estimated according to Fick's principle in patients with hepatic encephalopathy: evaluation of indocyanine green and D-sorbitol as test substances*". Hepatology.27, 666 (2012).
- [10] S .Keiding, E. Engsted, P. Ott. "*Sorbitol as a test substance for measurement of liver plasma flow in humans*". Hepatology, 28, 50 (2015).
- [11] DC .Yeh, M.C. Lin, T.J. Liu, F.K. P'Eng, "*Improving operative safety for cirrhotic liver resection*", British Journal Surgery, 88, 210 (2010).
- [12] Y. Kamiyama, A.H.Kwon, Y. Matsui, S.K. Ha-Kawa, "*Functional hepatic volume measured by technetium-99m-galactosyl-human serum albumin liver scintigraphy: comparison between hepatocyte volume and liver volume by computed tomography*". American Journal Gastroenterol, 96, 541 (2011).

- [13] W. Imsamran, K. Leelawat, T. Leelawat, Subwongcharoen *et al.*, "*Simple technique in the measurement of liver volume*", Journal Of The Medical Association Of Thailand, 86, 151 (2013).
- [14] J .Fehey, . N. R.Rose; H. Friedman, "*Manual of Clinical Laboratory immunology*", 3rd Ed., Mielee East Edition. 226 (2014).
- [15] A.Khalil, D. Tessier; T. Fulop, "*Liver volume in patients with or without chronic liver diseases*", Journal Biology Scientific, 54(11), 541 (2016).
- [16] N .Usuki, T. Miyamoto, "*Chronic hepatic disease: usefulness of serial CT examinations*", Journal of Computer Assisted Tomography, 26, 421 (2012).
- [17] K .Sandrasegaran, P.W. Kwo, D. DiGirolamo, *et al.*, "*Measurement of liver volume using spiral CT and the curved line and cubic spline algorithms: reproducibility and interobserver variation*", Abdominal Imaging, 24, 61 (2013).
- [18] M.Sheetz, & G.L. King, "*Molecular understanding of hyperglycemia's adverse effects for diabetic complications*", National Institutes of Health. JAMA, 288(20), 2579 (2015).
- [19] D .Dvornik, "*Aldose Reductase Inhibition: an Approach to the prevention of diabetic Complications*", McGraw Hill, New York, 368 (2014).
- [20] C.Karlsson, H. Jornvall., J. Hoog ., "*Sorbitol dehydrogenase: cDNA coding the rat enzyme; variations within the alcohol dehydrogenase famil independent of quaternary struture and metal content*", Europe. Journal. Biochemistry, 198, 761 (2011).

- [21] M.C. Delmas Beauvieux; E. Peuchant,.., "*Couchouron Short-term insulin therapy and normo glycemia. Effects on erythrocyte lipid peroxidation in NIDDM patients*", *Diabetes Care*, 20, 202 (2016).
- [22] D. Rastenyte, J .Tuomilehto.; P. Jousilahti,; *et al.*" *Diabetes Mellitus as a risk factor for death from stroke: prospective study of the middle aged Finnish population*", *Stroke*,27(2), 210 (1996).
- [23] J.Jin,W.Liao,W.Yao,R.Zhu,Y.Li,S.He., "*Aldo-keto Reductase Family 1. Member B 10 Mediates Liver Cancer Cell Proliferation through Sphingosine-1-Phosphate*". *Scientific Research*, 6, 22746 (2016).
- [24] T .Matsunaga, A. Suzuki, C. Kezuka, N. Okumura, K. Iguchi, I. Inoue, M. Soda," *Endo S, El-Kabbani O, Hara A, Ikari A. Aldo-keto reductase 1B10 promotes development of cisplatin resistance in gastrointestinal cancer cells through down-regulating peroxisome proliferator-activated receptor- γ -dependent mechanism*", *Chemical Biology Interaction*, 256, 53 (2016).
- [25] X .Wu, Li X, Fu Q, Cao Q, Chen X, Wang M, Yu J, Long J, Yao J, Liu H, Wang D, Liao R, Dong C. "*AKR1B1 promotes basal-like breast cancer progression by a positive feedback loop that activates the EMT program*", *Journal Experimental Medicine*, 214, 1065 (2017).
- [26] G .Molino, Battista S, Bar F, Garelo E, Avagnina P, Grosso M, Spalluto F. "*Determination of functional portal-systemic shunting in patients submit-ted to hepatic angiography*", *Liver*, 16:347-352. (2016).
- [27] M.D.Makoto Asada, M.D. Galambos ,"*Sorbitol Dehydrogenase and Hepatocellular Injury: An Experimental and Clinical Study*", *AGA Journal*, 44(5) 567. (2016)..