

COMPARISON ANALYTICAL BETWEEN CHOLESTEROL -7- α HYDROXYLASE AND FARNESOID X RECEPTOR SERUM AS DIAGNOSTIC TEST IN PATIENT WITH GALLSTONE

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(Received 12 March 2020, Revised 22 June 2020, Accepted 7 July 2020)

Foundation: Cholesterol -7- α hydroxylase protein is rate restricting in bile corrosive union has been explored to be related with gallbladder stone malady (GSD) and serum lipid levels, To assess on the clinical concentration of serum cholesterol 7- α hydroxylase by ROC bend as a test symptomatic test in gallstone diseases. **Methods:** Patients with gallstones were detailed , last conclusion was decided created off therapeutic times past then examinations, the level for serum of Cholesterol -7- α hydroxylase. ROC examination was utilized to decide the perfect higher reference extend cut-off esteem toward enhance sensitivity/specificity intended for GSD. The time of blood example group be situated to examine conceivable variety in comes about all through in work day. **Result :** The ROC examination generated a sensitivity/specificity of 98%/80% for Cholesterol -7- α hydroxylase and 90%/77% for Farnesoid X Receptor utilizing thirty ng/mL as the higher constrain of ordinary for serum Cholesterol -7- α hydroxylase when associated by way of all other patients. Of 146 patients. Serum Cholesterol -7- α hydroxylase levels were altogether higher in blood examples (P<0.05). **Conclusion:** Serum Cholesterol -7- α hydroxylase testing could be a basic, touchy, noninvasive, low-cost elective to other more commonly utilized tests for GSD

Key words : Cholesterol-7- α hydroxylase, gallstone, patient.

INTRODUCTION

The Gallstones be there a communal scientific discovery within the Spaghetti western populaces. A Ultrasound thinks about show cruel predominance proportions of (10–15%) in grown-up European, and of (3–5%) in African in addition to Asian populaces (Marschall HU and Einarsson C,2007). Additional than 80% of gallstone carriers are uninformed of their gallbladder malady (Attili AF,et al,1991) (Heaton KW, et al,1998), but around 1–2% per year of patients create impediments and require surgical procedure (Friedman GD et al,1998). The Contained by of US, the gallstone malady has the foremost common inpatient determination among gastrointestinal and liver illnesses (Russo MW et al,2004) Female sex, fruitfulness, and a family history for gallstone malady are emphatically related with the arrangement of cholesterol gallstones (Stampfer MJ et al,1992). Corpulence (Amaral JF, and Thompson WR,1985) as well too other components contributing to the metabolic disorder [Alberti KG et al,2005] such as dyslipidemia (in specific hyperlipoproteinemia sort IV [Nervi F et al,2006] with hypertriglyceridemia and HDL cholesterol), hyperinsulinemia-insulin resistance (Scragg RK et al,1998) or obvious sort 2 diabetes are

chance components for the advancement of gallstones, itself gathered to be a complication of the metabolic disorder. Farnesoid X receptor (FXR) capacities as the receptor for bile acids such as chenodeoxycholic corrosive (CDCA) (Chawla A, et al ,2001). Within the liver, bile corrosive is synthesized from cholesterol with cholesterol 7₋hydroxylase (CYP7A1) as the rate-limiting chemical . The expression of CYP7A1 is contrarily controlled by the translation calculate little heterodimer partner (SHP), the expression of which is improved by the ligand-bound FXR. Thus, bile corrosive smothers the expression of CYP7A1 in vivo through FXR, coming about in a diminish in its claim production. In the display consider, a serum cholesterol 7₋hydroxylase trail be there re-assessed used for retrieval, interfering then exactness within a setting for medical utilize now a expansive numeral a patients.

In the present study, the serum cholesterol 7-hydroxylase test was re-evaluated for recovery, interference and precision in the context of clinical use in a large number of patients. A commercial standard has now been used, and the use of potential internal standard (IS) described .An evaluation of the use of the cholesterol 7-hydroxylase test for diagnosis of GS in a clinical setting is reported, including an analysis of optimum cut-off

values and an assessment of the influence the time of the day of specimen collection has on results. We hope that these data will contribute to the optimization of the serum cholesterol 7-hydroxylase assay as a clinical test of BAM in patients with unexplained diarrhea. As a clinical test, more widespread adoption of serum cholesterol 7-hydroxylase analysis will aid in providing a routine diagnostic test for patients presenting with watery diarrhea.

SUBJECTS AND METHODS

The study was designed as a case control study that was carried out in the Department of Biochemistry at the Faculty of Medicine, University of Babylon in conjunction with the Babel Private Hospital. The subjects enrolled in the study were 280, these subjects categorized into two groups as following:

Patient group, which involves (140) of patients diagnosed with gallstone and and prepared for surgery as a definite treatment according to the surgical team decision, with an age range of 20-45 years composed from 46 males and 63 females and a mean of 43.48 ± 10.81 years.

Control group, includes (140) subjects comprised of apparently healthy volunteers and subjects who found to be normal as suggested by senior consultant during their attendance to medical Consultation Unit, with an age range of 21-45 years composed from 46 males and 94 females with an age range of 21-45 years and a mean of 41.31 ± 13.48 years.

The protocol was approved by the Institutional Review Board. After explaining the objectives of the study and obtaining written informed consent from all patients, baseline characteristics, and clinical data of participants were collected by interviewing and recorded using the study questionnaire.

Exclusion criteria involve hypertension, diabetes mellitus, renal, hepatic disorders, pregnancy, patients receiving drugs that could interfere with cholesterol, Antihyperlipidemic drugs (clofibrate).

Determination of serum concentrations of Cholesterol -7- α hydroxylase and for Farnesoid X Receptoand serum concentration based on solid phase competitive Sandwich-enzyme linked immunosorbent assay (ELISA) as prescribed earlier

Statistical analysis

All statistical analyses were performed using statistical package for social sciences (SPSS), version 17. Data were expressed as mean \pm SD. The normality of the distribution of all variables were assessed by the

analysis of variance t-test and Pearson correlation tests that have been used to determine the significant difference between the studied groups.. P values less than 0.05 were considered significant and less than 0.01 were considered highly significant (Norman, 2010).

Receiver Operating Characteristic (ROC) analysis was performed as a comprehensive way to assess the accuracy of the studied markers. The Area Under the Curve (AUC) provides a useful tool to compare different biomarkers. Whereas an AUC value close to 1 indicates an excellent diagnostic and predictive marker, a curve that lies close to the diagonal (AUC = 0.5) has no diagnostic significance. AUC close to 1 is always accompanied by satisfactory values of specificity and sensitivity of the biomarker (Hajian-Tilaki, 2013).

RESULTS

Association between CYP7A1 serum and GS

There was a significant difference in serum CYP7A1 level between studied group ($p= 0.0001$), and the highest level was in GS group as figure 1 revealed. Serum Farnesoid X Receptor (FXR) concentration

The serum level of FXR is significantly between studied group ($p= 0.0001$) as shown in figure 3, and it was significantly higher in patient group than in control group which was similar of (Otte K, et al, 2003).

The homeostasis of cholesterol was encouraged within a liver via a difficult arrangement of passageways, by the middle of that lies cholesterol 7-hydroxylase (CYP7A1), the proportion-limiting chemical within the change of cholesterol to bile corrosive of CYP7A1 movement was generally intervened through input hindrance via the bile-sensing farnesoid X receptor acceptance of little heterodimer accomplice. The FXR receptor moreover control the efflux of bile acids and phospholipids from the hepatocyte to the bile by up-regulating the bile salt send out pump (ABCB1)

In expansion there was critical positive relationship between serum level of CYP7A1 and FXR ($P < 0.001$, $r=0.86$) in all subject as figure 3 appeared, this positive relationship record our proposal that one of the causes for height of FXR was to neutralize the impact of CYP7A1.

The serum level of CYP71 is a sensitive biomarker in the context of Receiver Operating Characteristic (ROC) analysis, yet the it is not satisfactorily specific since it may affected my many conditions other than FXR with an AUC of 0.83 with sensitivity of (84%) and specificity of (62%) at a cut off value 14.7 pg/ml, as shown in Fig.

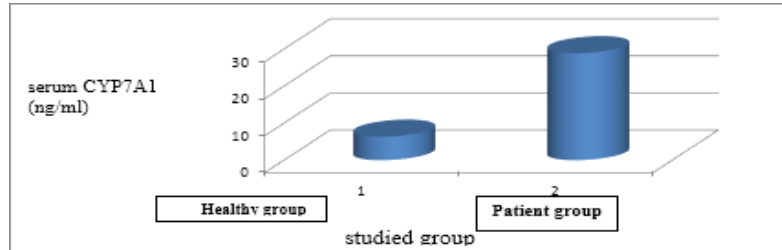


Fig. 1 : Mean of serum CYP7A1 concentration in studied group.

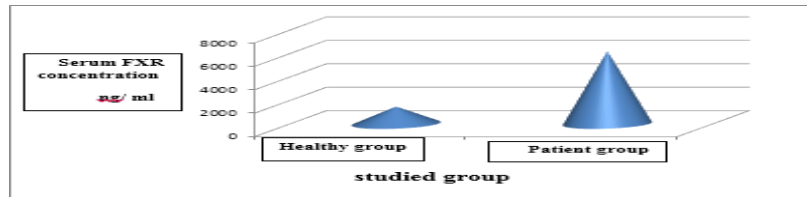


Fig. 2 : Serum FXR concentration (pg/ml) in studied group.

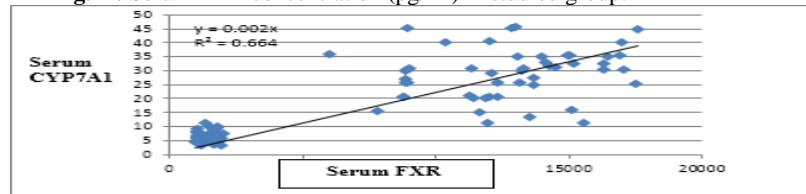


Fig. 3 : Correlation between serum level of CYP7A1 and FXR.

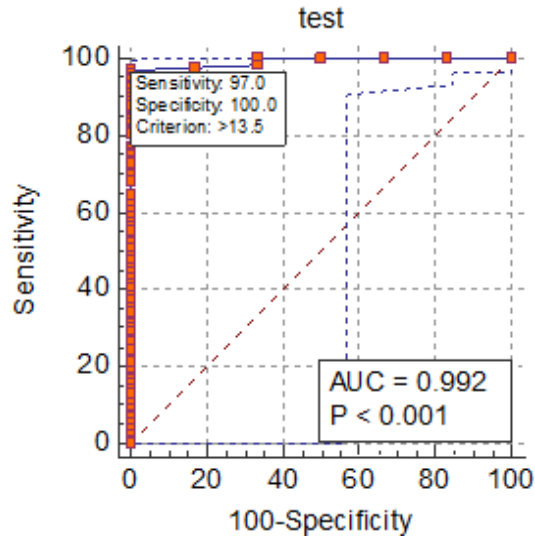


Fig. 4 : Receiver Operating Characteristic (ROC) curve of serum level of CYPA17 of patients group against control group, AUC: area under the curve

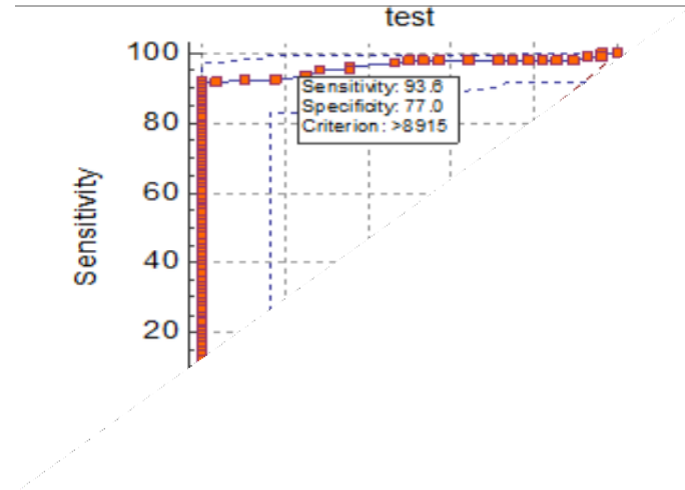


Fig. 5 : Receiver Operating Characteristic (ROC) curve of activity of ABC1 of patients group against control group, AUC: area under the curve

Discussion

The ROC test is right now the test of choice for the conclusion and estimation of GS . The trial was planned toward be there wonderfully touchy of it procedures the full bile corrosive held within the body above the seven-day time amid that a irritate bladder purge additional over 30 spells then the ileum is dared toward of reabsorb bile acids that were something else misplaced addicted to feces. The ROC test was accessible in our healing center and embraced at the caution of the doctor. In any case, after the past think about, the lion's share of the patients were explored by serum cyp7 trail as it were. Serum cyp7 is basically a trial of bile corrosive costs, that was appeared of a few ponders toward relate conversely by a ROC trial , with the foremost later affirmation via Bajor et al. Within that was show consider, a trial is re-evaluate aimed at procedural precision then appeared in the direction of exceedingly delicate (more prominent than 90%) for the determination of GS. A noteworthy numeral of the patients with IBS (9% of add up to investigated) was hoisted comes about. The affirmed of prior consider then had as of late been inspected broadly by Wedlake et al, who checked on other writing with thinks about affirming the GSD was illustrated in 10% to 32% of patients with diarrhea-predominant by the ROC trail Serum CYP7 is less particular intended for ilea illness than ROC since that is additionally influenced via bacteria colony through the bile salt de-conjugation within a little intestine , in the direction of the ROC particle was generally safe.

Generally, the 13of patients through little bowel colonization is elevated serum levels ofcyp7. That the comparable toward of 14C glycocholate inhalation trial is utilized together of trial used for little intestinal bacteria colony then the ileal disease. In spite of the fact that facts used for specific be there moderately, a trial be there exceedingly delicate for GSI. Besides additional circumstances the rise toward GS, like ilea resection, postcholecystectomy the runs then a diabetes, is rapid to distinguished as of the essential pathology.

Conclusion

In spite of the fact that the ROC trial is appeared as strong trial for the bile corrosive mala-bsorption, that the utilize of the gamma radioactivity then a quiet period included could clear block the situation of programmed determination the choose a trial of GS, it is moderately unassuming, actual trial as serum CYP₇ that accessible. the expanding utilize then accessibility of quantity spectroscopy in symptomatic research facilities then a later reported by way of (Camilleri et al), that like a serum CYP₇ test is gotten to be broadly accessible.

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