



A CLINICAL AND BIOCHEMICAL STUDY OF SERUM PROTEIN PROFILES IN CASES OF OBSTRUCTIVE JAUNDICE

KEYWORDS

obstructive jaundice, p value, serum proteins, albumin.

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ABSTRACT 1. *Background; obstruction to the flow of bile can impair liver function in several ways . which included synthetic and excretory function of liver. Estimation of serum proteins is one of the methods of estimation of chronicity and severity of liver damage and predicts out come in such cases.*

2. *Methods; serum protein profiles of 40 patients with surgical jaundice was studied over a period of 18 months. Variations in protein concentrations due to malignant and benign causes were analysed mainly with regard to albumin, prothrombin time, total proteins globulins and A;G ratio.*

3. *Results; total serum proteins were decreased in patients with obstructive jaundice due to any cause compared with normal population. Serum protein changes due to malignant obstruction is similar to benign cause of obstruction.*

4. *Conclusion; estimation of various serum protein changes in obstructive jaundice is very important as it may influence management of patients and predict outcome disease because significant changes in these indicates irreversible changes in liver which are associated with bad prognosis in obstructive jaundice.*

Introduction;

Obstructive Jaundice is a common surgical problem that occurs when there is an obstruction to the passage of bile from liver to intestine . It is among the most challenging conditions managed by general surgeons and contributes significantly to high morbidity and mortality . As patients with obstructive jaundice have high morbidity and mortality, early diagnosis of the cause of obstruction is very important especially in malignant cases, as resection is only possible at that stage . Jaundice due to biliary obstruction may be caused by a heterogeneous group of diseases that include both benign and malignant conditions . The common etiologies of obstructive jaundice have been reported to vary from one centre to another and from one individual to another . Obstructive jaundice is not a definitive diagnosis and early investigation to elucidate the precise etiology is of great importance because pathological changes (e.g. secondary biliary cirrhosis) can occur if obstruction is unrelieved . A vast array of invasive and non invasive diagnostic tests is available to diagnose and establish the etiology of surgical jaundice . Invasive tests may cause cholangitis and imaging techniques like computed tomography (CT) scan, PTC, ERCP and MRCP are expensive and are not readily available in most centers in developing countries , and ultrasonography remains the only diagnostic test available most commonly. The management of obstructive jaundice poses diagnostic and therapeutic challenges to general surgeons practicing in resource-limited countries . Late presentation of the disease coupled with lack of modern diagnostic and therapeutic facilities are among the hallmarks of the disease in developing countries . Surgery in jaundiced patients is associated with a higher risk of postoperative complications compared with surgery in non jaundiced patients . These complications primarily consist of septic complications (cholangitis, abscesses, and leakage), hemorrhage, impaired wound healing and renal disorders. It has been reported that obstructive jaundice

continues to be associated with significant morbidity and mortality despite recent advances both in preoperative diagnosis and postoperative care . Understanding factors responsible for increased morbidity and mortality in these patients will better guide appropriate management and lead to improved survival

Aims and Objectives;

Aims and objectives are to study serum protein changes in patients with obstructive jaundice due both to benign and malignant causes of biliary system , and its outcome due to changes in serum proteins .

Material and Methods;

a retrospective analysis 40 patients who presented with or referred to Osmania general hospital, Hyderabad with jaundice are studied and analysed over a period of 18 months are included in this study. The patients are selected randomly. Patients are thoroughly examined physically and appropriate radiological and other investigations done. All patients serum proteins estimations including total proteins, albumin, globulins, and clotting factors which are synthesized by liver, are done by various methods. These include biuret method for proteins, agglutinin tests for globulins, and clotting factors were also analysed by electrophoretic studies. Other proteins such as ceruloplasmin, haptoglobin, lipoproteins, retinol binding protein ,serum transferrin, thyroxine binding proteins were not studied as they were not available at our center or we felt that clinically these are not significant for the management of a case of obstructive jaundice. These patients are grouped into benign causes and malignant causes of case 20 each and results analysed.

Inclusion Criteria;

1. patients between 20- 75 years of age,
2. only cases which are documented to have obstructive jaundice clinically and proven by radiological investigations

are included
3.patients with positive direct serum bilirubin

Exclusion Criteria;

1. patients with drainage procedure on CBD,
2. medical jaundice,
3. patients below 20 years and above 25 years.

ANALYSIS OF RESULTS and ABSERVATIONS

1.TOTAL PROTEINS:

Group A (Benign): Number of items= 20

5.10 5.20 5.60 5.90 6.00 6.00 6.30 6.40 6.40 6.50 6.60
6.60 6.70 6.80 6.90 6.90 7.00 7.00 7.20 7.20

Mean = 6.41

95% confidence interval for Mean: 6.077 thru 6.753

Standard Deviation = 0.615

Hi = 7.20 Low = 5.10

Median = 6.55

Average Absolute Deviation from Median = 0.475

Group B(Malignant): Number of items= 20

4.80 5.50 5.50 5.60 5.70 5.70 5.80 6.20 6.20 6.30 6.40
6.70 6.70 6.80 6.80 7.30 7.30 7.60 7.70 8.00

Mean = 6.43

95% confidence interval for Mean: 6.092 thru 6.768

Standard Deviation = 0.860

Hi = 8.00 Low = 4.80

Median = 6.35

Average Absolute Deviation from Median = 0.700

t=-0.635E-01

sdev= 0.747

degrees of freedom = 38

The probability of this result, assuming the null hypothesis, is 0.950

2.ALBUMIN:

Group A(Benign): Number of items= 20

2.70 2.90 3.00 3.20 3.40 3.40 3.40 3.50 3.50 3.60 3.60
3.70 3.80 3.80 3.80 3.80 3.90 3.90 3.90 4.00

Mean = 3.54

95% confidence interval for Mean: 3.326 thru 3.754

Standard Deviation = 0.362

Hi = 4.00 Low = 2.70

Median = 3.60

Average Absolute Deviation from Median = 0.280

Group B(Malignant): Number of items= 20

2.00 2.30 2.40 2.40 2.60 2.60 2.60 2.70 2.70 2.90 2.90
2.90 3.00 3.00 3.10 3.10 3.30 3.70 4.10 4.20

Mean = 2.92

95% confidence interval for Mean: 2.711 thru 3.139

Standard Deviation = 0.564

Hi = 4.20 Low = 2.00

Median = 2.90

Average Absolute Deviation from Median = 0.405

t= 4.11

sdev= 0.474

degrees of freedom = 38

The probability of this result, assuming the null hypothesis, is 0.000

3. A:G RATIO:

Group A(Benign): Number of items= 20

0.740 0.750 1.06 1.09 1.11 1.12 1.13 1.20 1.20 1.22 1.23
1.25 1.25 1.30 1.33 1.45 1.52 1.72 1.85 2.25

Mean = 1.29

95% confidence interval for Mean: 1.150 thru 1.427

Standard Deviation = 0.348

Hi = 2.25 Low = 0.740

Median = 1.23

Average Absolute Deviation from Median = 0.226

Group B(Malignant): Number of items= 20

0.450 0.540 0.550 0.600 0.610 0.710 0.740 0.820 0.830
0.860 0.900 0.960 0.970 1.00 1.00 1.03 1.05 1.13 1.20
1.50

Mean = 0.872

95% confidence interval for Mean: 0.7339 thru 1.011

Standard Deviation = 0.257

Hi = 1.50 Low = 0.450

Median = 0.880

Average Absolute Deviation from Median = 0.202

t= 4.30

sdev= 0.306

degrees of freedom = 38

The probability of this result, assuming the null hypothesis, is 0.000

PROTHROMBIN TIME

Group A(Benign): Number of items= 20

14.0 14.0 15.0 16.0 16.0 16.0 16.0 16.0 18.0 18.0 18.0
18.0 18.0 19.0 19.0 20.0 20.7 21.0 21.0 45.0

Mean = 18.9

95% confidence interval for Mean: 16.77 thru 21.10

Standard Deviation = 6.50

Hi = 45.0 Low = 14.0

Median = 18.0

Average Absolute Deviation from Median = 3.04

Group B(Malignant): Number of items= 20

17.0 18.0 18.0 18.0 18.0 18.0 18.0 18.0 18.0 18.0 19.0
19.0 20.0 20.0 21.0 21.0 21.0 21.0 22.0 24.0

Mean = 19.4

95% confidence interval for Mean: 17.19 thru 21.51

Standard Deviation = 1.81

Hi = 24.0 Low = 17.0

Median = 18.5

Average Absolute Deviation from Median = 1.45

t=-0.275

sdev= 4.77

degrees of freedom = 38

The probability of this result, assuming the null hypothesis, is 0.785

GLOBULINS:

Group A(Benign): Number of items= 20

1.60 2.10 2.20 2.40 2.40 2.40 2.50 2.90 3.00 3.00 3.00
3.00 3.10 3.10 3.10 3.20 3.20 3.40 3.90 4.00

Mean = 2.88

95% confidence interval for Mean: 2.567 thru 3.183

Standard Deviation = 0.586

Hi = 4.00 Low = 1.60

Median = 3.00

Average Absolute Deviation from Median = 0.425

Group B(Malignant): Number of items= 20

2.50 2.80 2.80 2.90 3.00 3.00 3.10 3.10 3.10 3.40
3.40 3.50 3.60 3.90 4.20 4.20 4.30 5.00 5.30

Mean = 3.49

95% confidence interval for Mean: 3.187 thru 3.803

Standard Deviation = 0.765

Hi = 5.30 Low = 2.50

Median = 3.25

Average Absolute Deviation from Median = 0.585

$t = -2.88$

$sdev = 0.681$

degrees of freedom = 38

The probability of this result, assuming the null hypothesis, is 0.007

DISCUSSION

The liver plays a critical role in metabolism and assimilation of nutrients. It is central in orchestration of protein and carbohydrate metabolism. Any defect or disease of liver will result in significant metabolic derangements. Progression of liver dysfunction results not only in metabolic derangement from decrease in number of functioning hepatic cells but also in shunting of portal blood, which decreases the delivery of nutrients, growth factors and hormones to the remaining cells.

The liver synthesizes the majority of proteins that circulate in the plasma, including albumin and most of the globulins other than gamma globulins. Albumin provides most of the oncotic pressure of plasma and is a carrier for drugs and endogenous hydrophobic compounds such as unconjugated bilirubin. Globulins include the coagulation factors: fibrinogen, prothrombin (factor II), and factors V, VII, IX and X. Factors II, VII, IX and X are vitamin K-dependent. Availability of vitamin K, a fat-soluble vitamin, requires adequate bile salts for the vitamin's absorption.

When liver function is deranged by different disease processes, different functions of liver change mainly synthetic functions which is reflected by alteration in many liver function tests.

Most serum proteins are synthesized within the liver, the major exception being the immunoglobulins. Therefore they have been used as a measure of hepatic synthetic capacity, however many extrahepatic factors, in particular elimination, influence the serum levels of all serum proteins.

The most frequently used parameters of synthetic capacity are clotting factors and serum albumin.

The liver is the major site of synthesis of blood clotting factors. Coagulation defects are frequent in chronic liver disease, they do not universally reflect impaired synthetic capacity but may also be related to intravascular coagulation and vitamin K malabsorption. Production of factors II, VII, IX, X vitamin K dependent.

The best studied parameter is Prothrombin time(PT), it is part of several prognostic indices and determined serially carries prognostic information on its own in e.g. paracetamol poisoning.

Individual clotting factors have also been evaluated as diagnostic tools, thus factor VII was found to be an excellent measure of hepatic synthetic function. Factor V is used to predict timing of liver transplantation in fulminant hepatic failure. Factor V levels are also good predictors of survival in liver transplantation in adults and children. Fibrinogen levels are usually normal or slightly elevated in mild liver disease

but markedly decreased in massive hepatocellular damage. There is disagreement whether or not preoperative coagulation abnormalities predict intra operative blood loss, blood product use and survival in liver transplantation.

Determination of Prothrombin time is routine, its value should be incorporated into diagnostic scores where appropriate.

Like clotting factors albumin is synthesized exclusively in liver. Its serum concentration is dependent upon the volume of distribution and there can be extrahepatic loss leading to low albumin levels in the absence of structural liver disease. Albumin is not a very sensitive indicator of synthetic function since a 50% reduction in synthesis rate induces only a 20% fall in serum levels. Because of its long half life of 20 days it does not indicate synthetic function in acute liver disease.

Prealbumin may be a more sensitive indicator than albumin and other conventional LFTs. It correlates with Child's classification and Galactose elimination capacity but it has yet to prove its superiority to Albumin determinations. Albumin level is poor screening test but should be measured where there is suspicion of malnutrition and/or chronic liver disease. Preoperative albumin level is said to be good indicator of mortality, morbidity and post operative recovery in patients with liver disease and obstructive jaundice. Coming to the globulins in a case of obstructive jaundice vary widely depending on the clinical situation. Normally the level of and globulins will increase and globulins remains the same. But if the patient is in biliary sepsis the level of globulins will be very high.

The A:G ratio(albumin to globulin) in patients of obstructive jaundice vary with relative proportions of albumin and globulins. Routinely the A:G ratio will be reversed as there is decrease in serum albumin levels with increase in levels of globulins. The change in ratio depends on change in relative proportions of these proteins.

CONCLUSIONS:

1. The level of total serum proteins in patient with obstructive jaundice is less compared to standard value of normal population and it appears to be statistically significant (P value less than 0.005).
2. The level of total serum proteins in cases of malignant obstructive jaundice is almost equal to that of benign cases of obstructive jaundice.
3. The level of total serum albumin in patient with obstructive jaundice is less compared to standard value of normal population but it appears to be statistically significant (P value less than 0.005).
4. The level of serum albumin in cases of malignant obstructive jaundice is less compared to that of benign obstructive jaundice and that is statistically significant.(P value less than 0.005)
5. There is decrease in A:G ratio observed in all cases of obstructive jaundice compared to standard values.
6. There is significant decrease (reversal) of A:G ratio in malignant obstructive jaundice compared to that of benign ones (P value less than 0.005).
7. when compared to standard values there is no significant alteration observed in prothrombin time values of cases of obstructive jaundice.either due to malignant or benign cause.
8. There is no significant change in values of Prothrombin time in cases of benign and malignant obstructive jaun-

dice (P value is 0.785).

9. There is no significant change in levels of globulins in cases of benign and malignant cases of obstructive jaundice (P value is 0.007).

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