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Evaluation of Liver panel and Electrolytes in Individuals with Isolated Hyperbilirubinemia

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ABSTRACT

Background: An elevation in serum bilirubin levels without significant changes in liver enzymes or other biochemical markers, presents a unique diagnostic challenge. In evaluating these patients, liver enzyme levels play a key role in differentiating between hepatic and non-hepatic causes of hyperbilirubinemia.

Methodology: A cross-sectional study was conducted on 200 patients with isolated hyperbilirubinemia at Raipur Institute of Medical Science & Hospital, Chhattisgarh, over two years. Patients aged 18 and above were included. Data were analysed using SPSS version 20, with descriptive statistics (mean & SD), and a p-value < 0.05 considered significant.

Result: The study included 200 subjects (63% female, 37% male) with elevated bilirubin levels, with a mean age of 34.23 ± 15.56 years. Total bilirubin was 15.34 ± 8.54 mg/dl. Significant differences were found between genders for direct bilirubin, ALT, creatinine, and urea.

Conclusion: Assessing bilirubin, liver enzymes, and electrolytes in isolated hyperbilirubinemia aids in differentiating benign conditions from more serious ones.

1. INTRODUCTION

Isolated hyperbilirubinemia is a condition characterized by an elevation in serum bilirubin levels without a significant increase in other liver function tests. Bilirubin, a byproduct of red blood cell breakdown, is normally processed by the liver and excreted as bile (1). However, when this process is disrupted, bilirubin accumulates in the bloodstream, resulting in jaundice (yellowing of the skin and eyes) (2). Hyperbilirubinemia is defined by an increase in the concentration of bilirubin in the bloodstream, which may lead to jaundice. Bilirubin is a yellow compound produced from the breakdown of hemoglobin in red blood cells. The liver processes bilirubin, making it water-soluble so that it can be excreted in bile (3). The elevation can be either unconjugated or conjugated bilirubin, and each has different clinical implications. Isolated hyperbilirubinemia can be a manifestation of several benign conditions, but its differential diagnosis is wide and should be thoroughly evaluated. Gilbert syndrome is usually asymptomatic, and jaundice may only be apparent during periods of heightened bilirubin production or stress (4). Liver enzymes such as alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), and gamma-glutamyl transferase (GGT) help in determining whether liver injury or dysfunction is present. However, in cases of isolated hyperbilirubinemia, these enzymes may remain normal, further suggesting that the bilirubin elevation is due to non-hepatic factors or benign conditions like Gilbert's syndrome (5). In addition to liver enzymes, electrolyte levels particularly sodium, potassium, chloride, and bicarbonate are often assessed (6). Electrolyte imbalances can occur as a result of various underlying pathologies, including those that affect liver function or the metabolism of bilirubin. By evaluating the full spectrum of liver enzymes and electrolytes, healthcare providers can better differentiate between various causes of hyperbilirubinemia and tailor management strategies appropriately (7). Understanding the interplay between bilirubin levels, liver enzyme activities, and electrolyte balance is crucial for diagnosing the root cause of isolated hyperbilirubinemia (8). This assessment helps to guide clinical decision-making and avoid unnecessary treatments for benign conditions. So, looking into above facts the present study has planned to evaluate hyperbilirubinemia, liver enzymes, and electrolytes in individuals with isolated hyperbilirubinemia

2. METHODOLOGY

A prospective observational cross-sectional type of study was conducted on total 200 clinically diagnosed patients of Isolated Hyperbilirubinemia in the Department of Biochemistry at Raipur Institute of Medical Science & Hospital, Raipur, Chhattisgarh in a duration of two years. Present study has obtained ethical approval from Institutional Ethical Committee from Raipur Institute of Medical Science & Hospital, Raipur, Chhattisgarh. Written and verbal consent were taken from all the participants.

Study Population: Patients diagnosed with isolated hyperbilirubinemia with concerned underlying cause of ≥18 years ages with following inclusion criteria.

Inclusion Criteria:

- Subject who was willing to participate.
- Above of 18 years of age groups of either sex.
- Clinically diagnosed patients of Hyperbilirubinemia.

Exclusion criteria:

- A non-cooperative and not willing subjects.
- Diagnosed cases of liver disease such as Liver cirrhosis, viral hepatitis etc.
- Pregnant women and individuals under 18 years
- Any venerable disorders such as HIV and any STDs.
- Subjects, who have routine habits Smoking, Nicotine and alcohol consumption

Sample size calculation: A sample size of at least **200 patients** with isolated hyperbilirubinemia were targeted to ensure statistical power. The sample size was determined using power analysis based on the expected effect size and the desired confidence level (95%) with an acceptable margin of error (5%).

3. SAMPLE COLLECTION AND ANALYSIS

Under aseptic precautions 5ml of the patient's intra-venous blood was obtained in fasting state and centrifuged at 4000 rpm for 8-10 minutes to obtained serum sample. Liver profile (Bilirubin, ALT, AST & ALP) and Blood Urea and Creatinine levels were estimated by ERBA EM-200 fully automated clinical chemistry analyser. Serum electrolyte levels were measured using ion-selective electrodes (ISE) in ERBA EM-200 analyser.

Study tools: Data were collected in case record form (CRF). The CRF comprised of details regarding diagnosis, cause, medication and serum biochemical marker values.

Statistical Analysis: The data were entered into Microsoft office excel and analyzed by Statistical Package for Social Sciences (SPSS) version 21 for windows software. Descriptive statistics were reported in the form of mean, standard deviation. Normal distribution of data was checked by Shapiro – Wilk test. Comparison between two groups of serum biochemical markers was done by independent t-test. Spearman correlation tests was used to examine the relationship between bilirubin levels and other variables such as LFTs and electrolytes. P-value < 0.05 was considered as statistically significant.

Results: The present study has included total of 200 subjects with increased bilirubin concentration. Among 200 subjects, 63% were Female and 37% male. The mean age of the subjects was 34.23 ± 15.56 years. The average mean of Total bilirubin is 15.34 ± 8.54 mg/dl, Direct bilirubin is 0.35 ± 0.22 mg/dl and Indirect bilirubin is 14.99 ± 8.57 mg/dl. The present study also compared the data between the two genders i.e., Male and Female and we found increased levels of most of the biochemical parameters but there is a significant difference observed in levels of direct bilirubin, ALT, Creatinine and Urea.

Figure-1: Gender distribution of Study Participants (N=200)

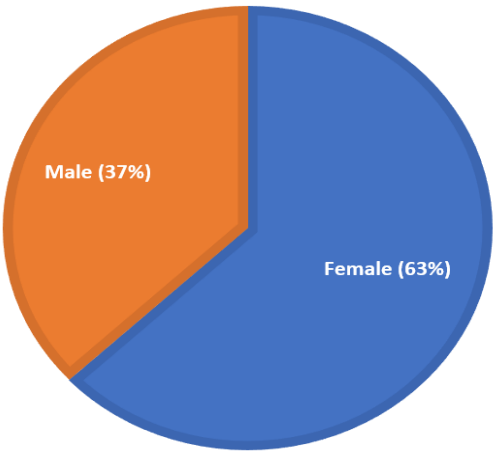

Table-1: Biomarkers characteristic for Isolated hyperbilirubinemia

Parameters	**Isolated Hyperbilirubinemia (N=200)**
	(Mean ± SD)
Age (Years)	34.23 ± 15.56
Total Bilirubin (mg/dl)	15.34 ± 8.54
Direct Bilirubin (mg/dl)	0.35 ± 0.22
Indirect Bilirubin (mg/dl)	14.99 ± 8.57
ALT (IU/L)	20.63 ± 5.51
AST (IU/L)	24.80 ± 4.77
ALP (IU/L)	75.63 ± 13.51
Total Protein (gm/dl)	7.51 ± 0.28
Albumin (gm/dl)	4.62 ± 0.26
Urea (mg/dl)	22.45 ± 6.70
Creatinine (mg/dl)	0.87 ± 0.13
Sodium (mEq/L)	139.33 ± 2.06
Potassium (mEq/L)	4.05 ± 0.29
Chloride (mEq/L)	118 ± 0.05

Table-1: Biomarkers characteristic for Isolated hyperbilirubinemia in Male and female.

Parameters	**Male (N=73)**		**Female (127)**		***P value***
	(Mean ± SD)	**SEM**	**(Mean ± SD)**	**SEM**	
Age (Years)	35.81 ± 17.31	1.73	33.43 ± 14.61	1.46	0.29
Total Bilirubin (mg/dl)	15.96 ± 9.19	0.91	15.02 ± 8.21	0.82	0.44
Direct Bilirubin (mg/dl)	0.39 ± 0.33	0.03	0.32 ± 0.13	0.01	0.04*
Indirect Bilirubin (mg/dl)	15.57 ± 9.22	0.92	14.70 ± 8.25	0.82	0.44

ALT (IU/L)	21.95 ± 5.48	0.54	19.96 ± 5.43	0.54	0.01*
AST (IU/L)	24.43 ± 5.36	0.53	24.98 ± 4.46	0.44	0.43
ALP (IU/L)	96.52 ± 23.13	2.31	94.99 ± 22.17	2.21	0.60
Total Protein (gm/dl)	7.54 ± 0.28	0.02	7.50 ± 0.28	0.02	0.31
Albumin (gm/dl)	4.69 ± 0.22	0.02	4.58 ± 0.28	0.02	0.002*
Urea (mg/dl)	24.50 ± 6.62	0.66	21.41 ± 6.53	0.65	0.001*
Creatinine (mg/dl)	0.94 ±0.10	0.01	0.83 ± 0.12	0.01	0.0001**
Sodium (mEq/L)	139.07 ± 2.29	0.22	139.46 ± 1.93	0.19	0.19
Potassium (mEq/L)	4.11 ± 0.31	0.03	4.02 ± 0.27	0.02	0.02*
Chloride (mEq/L)	118 ± 0.06	0.01	118 ± 0.05	0.01	1.0

Unpaired t test (P) value= **= P<0.001, *= P<0.05, P>0.05# (not significant)

4. DISCUSSION

Unconjugated hyperbilirubinemia is primarily due to either increased production or decreased clearance of bilirubin. Increased production is due to increases red blood cell turnover and decreased clearance is due to genetic disorders like Gilbert syndrome, Crigler-Najjar syndrome, or hepatocellular dysfunction [9]. Gilbert syndrome is one of the most prevalent causes of isolated unconjugated hyperbilirubinemia. It is a mild, genetic condition where there is reduced activity of the enzyme UDP-glucuronosyltransferase. This results in decreased conjugation of bilirubin and intermittent elevation of unconjugated bilirubin, especially during times of stress, fasting, or illness [10]. In adults, hyperbilirubinemia is commonly seen in liver or gallbladder diseases. Gilbert's syndrome may also cause isolated indirect hyperbilirubinemia but its prevalence is 6% [10]. We have gathered the total 200 patient laboratory data mainly focused on hyperbilirubinemia and represented in the form of average mean in this study. In the clinical context, evaluating bilirubin levels alongside liver enzymes and electrolytes is essential for differentiating between causes of isolated hyperbilirubinemia and determining its underlying aetiology. **Conjugated hyperbilirubinemia** points to **hepatic** or **post-hepatic** causes, such as hepatocellular injury (e.g., viral hepatitis, alcoholic liver disease) or biliary obstruction (e.g., gallstones, cholangiocarcinoma). In the case of isolated hyperbilirubinemia, if direct bilirubin is elevated with minimal changes in liver enzymes, it may indicate a benign condition, like Dubin-Johnson syndrome or Rotor syndrome, which are inherited disorders of bilirubin metabolism [11]. The present study has observed highly increased total and indirect bilirubin concentration. Murtaza et al [12] have reported the same pattern of bilirubin in their case study**.** However, in gender-based observation we did not find any such difference among male and female. In a study by Kotal et al. [13], mechanism behind fasting-induced hyperbilirubinemia was studied in Gunn rat models as Gunn rats have inherited absence of UDP-Glucuronyl Transferase enzyme. Their study revealed that the fasting results in reduced intestinal motility leading to decreased elimination of bile pigments and causing their enhanced enterohepatic circulation and increased reflux of bilirubin in plasma.

Liver enzymes, primarily alanine aminotransferase (ALT), aspartate aminotransferase (AST), and alkaline phosphatase (ALP) provide important clues for determining liver injury and dysfunction. Whereas, ALT and AST are indicators of hepatocellular damage. Elevated levels usually point to hepatocellular injury and A**LP is** associated with biliary tract disease or obstruction [14]. The present study has observed a normal level of liver enzymes and among males and females; levels are slightly increased in females but within the normal range. In patients with **isolated hyperbilirubinemia**, electrolyte imbalances are unlikely to be directly related to bilirubin levels unless there is a complicating factor, such as dehydration, liver failure, or metabolic disturbance [15]. However, in cases where liver function is compromised then disturbances in electrolytes might be seen. In contrast, in an older individual, or one with risk factors for liver disease (e.g., alcohol use, obesity, diabetes), the possibility of liver disease should be considered even if liver enzymes are initially normal. Further testing, such as **ultrasound, hepatitis panels**, or **liver biopsy**, may be necessary to evaluate for subclinical liver disease or early hepatic dysfunction [16].

Conclusion

- Evaluating bilirubin levels, liver enzymes, and electrolytes in individuals with isolated hyperbilirubinemia helps in differentiating benign from more serious conditions.
- The present study results provided valuable insights into the interplay between bilirubin levels, liver function, and electrolytes in individuals with isolated hyperbilirubinemia.
- These findings may contribute to improving diagnostic strategies and treatment protocols for managing patients with

elevated bilirubin levels, particularly in distinguishing benign conditions from more serious hepatic disorders.

Limitations

- The study may be limited by the inability to capture all potential causes of isolated hyperbilirubinemia.

There may be selection bias in recruitment, especially if participants with comorbidities are excluded.

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