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SERUM BILIRUBIN AND GAMMA- GLUTAMYL TRANSFERASE IN WOMEN SUFFERING FROM MIGRAINE.

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ABSTRACT

BACKGROUND: Migraine is a common health issue of predominantly women than men. It affects the lifestyle of person. New biomarkers need to be addressed for an old problem.

OBJECTIVE: To study serum bilirubin and liver enzyme in women suffering from migraine at our tertiary care hospital. **STUDY DESIGN:** A cross- sectional study, **STUDY PLACE:** Out- patient and Medicine Department, Isra University Hospital from March 2024 to January 2025. **METHODS:** One hundred migraine cases and controls were selected according criteria. Women of age 20- 40 years were selected. Visual Analogue Scale (VAS) was used for migraine severity. Volunteers were asked for blood samples. Blood samples were collected in Na-F containing tubes for detecting liver function tests analyzed on Cobas Roche Analyzer. Study variables and statistical analysis was performed on SPSS (22.0) using Student t-test and correlations by Spearman`s testing. Correlation scatter plots were developed on Microsoft Excel sheet. Statistical analysis was taken at $P \leq 0.05$ as significant. **RESULTS:** Total (TB), direct (DB) and Indirect bilirubin (IB) among migraine patients and controls were found 1.01±0.32 vs. 1.35±0.07 mg/dl (P=0.0003), 0.61±0.02 vs. 0.77±0.08 mg/dl (P=0.0002) and 0.13±0.02 vs. 0.28±0.05 mg/dl (P=0.003) respectively. GGT in migraine patients was 77.6±9.3 IU compared to 35.3±5.07 IU in controls. TB, DB and IB show negative correlation with VSA migraine severity while GGT exhibited positive correlation. **CONCLUSION:** The present study shows reveals bilirubin levels and elevated gamma glutamyl transferase (GGT) in women suffering from migraine.

KEY WORDS: Bilirubin, Women, Migraine, Liver Enzymes

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INTRODUCTION

Migraine is a vascular type of headache. Vascular spasm is the underlying mechanism of unknown etiology. Migraine affects 12 – 15% adults in Western countries. Migraine complainers are ever increasing since last decades. Women complain of headache that is often throbbing in nature. Headache may be associated with nausea, tearing, vertigo, tinnitus, photophobia, phonophobia and in severe cases with hemiplgeia.[1,2] Migraines may be acute, episodic and chronic. Acute migraine is self-limiting condition. Migraine of adulthood has myriad clinical presentation and disability, safety and efficacy of drug therapy. Migraine causes

substantial decline in working ability. In women, it causes functional disability and may worse academic performance. Women have often increased risk of depression compared to age peers. About 7 million adults are affected by migraine in United States. Globally, headache is reported in 60% children and adults, of whom 7.7%– 9.1% have migraine.[1,2] Biochemical markers for migraine have been reported by studies[2,3] that play role in migraine and assessing clinical risk factors. Bilirubin is reported as a clinical risk factor in previous studies. Bilirubin is a thought as clinical risk factor. It is a toxic metabolite of heme catabolism & produced by phagocytic cells. Bilirubin shows anti – oxidant and cytoprotective effects studies.[1,4] A previous study[5] reported the bilirubin levels correlated with the arterial stiffness in cardiac disease patients. Another past study[6] associated the renal filtration rate with serum bilirubin, reportedly low bilirubin levels were found in chronic kidney disease. Low serum bilirubin[1] is proved with systemic hypertension and multiple sclerosis. Few studies[1-3] have analyzed the correlation of serum bilirubin with migraine. The present study is designed to study the serum bilirubin and liver enzymes - gamma glutamyl transferase in migraine patients. The serum bilirubin and GGT were compared with migraine severity using visual analogue scale (VAS) presenting at outpatient and medical wards. The objective of research was to estimate bilirubin and GGT in migraine and correlate with the visual analogue scale.

MATERIAL AND METHODS

A cross sectional study was conducted at the Department of Out- patient and Medical wards, Isra University Hospital from March 2024 to January 2025. Migraine was diagnosed by consultant physician. Ethical review committee approval for study was taken for conducting prospective research. "Sampling-proportions" using Rao software was used for calculating patient sample. Equal number of age and weight matched healthy women were taken as controls. Migraine was diagnosed as suggested by guidelines.[9] Severity of headache was categorized by Visual Analogue Scale (VAS).[10] 0 – 10 numeric pain rating VAS scale was used. i).0 – as no–pain, ii). 1 –5 as moderate– pain and iii) 6 – 10 as severe– pain. A sample of 100 hundred migraine case and 100 controls were selected according to criteria. Women of age 20- 40 years, complaining of migraine were selected. Women suffering from concomitant disease were excluded. Malnourished, hypertensive, diabetic and those suffering chronic illness were excluded. Volunteers were informed about the purpose of study and for blood sampling on volunteer basis only. A proforma was designed for patient data. Vitals were noted and entered. 5 ml blood was taken by disposable syringe from ante cubital vein. Blood samples were collected in Na-F containing tubes for detecting liver function tests analyzed on Cobas Roche Analyzer. Study variables and statistical analysis was done on SPSS (22.0) using Student t-test and correlations Spearman`s testing. Correlation scatter plots were developed on Microsoft Excel sheet. Statistical analysis was taken at $P \leq 0.05$ as significant. Scatter plots were plotted on Microsoft Excel sheet.

RESULTS

Age, body weight and blood pressure findings of cases and controls of study are shown in Table – 1. Table 2 depicts the liver function test findings, showing significant differences in total, direct and indirect bilirubin level and γ- Glutamyl Transferase among patients and controls ($P<0.001$). Total (TB), direct (DB) and Indirect bilirubin (IB) among migraine patients and controls were found 1.01±0.32 and 1.35±0.07 mg/dl ($P=0.0003$), 0.61±0.02 and 0.77±0.08 mg/dl ($P=0.0002$), 0.13±0.02 and 0.28±0.05 mg/dl ($P=0.003$) respectively. GGT in migraine patients was 77.6±9.3 IU

compared to 35.3±5.07 IU in controls. TB, DB and IB show negative correlation with VSA migraine severity (Scatter plots 1), while γ –GT exhibited positive correlation shown table 3 (Scatter plot 2).

Table 1. Patient and control data

	Patients	Control	P-value
Age (years)	39.2±9.5	38.9±11.4	0.081
Body weight (kg)	76.5±10.9	75.3±11.3	0.061
Systolic BP (mmHg)	119.51±9.31	117.3±8.31	0.072
Diastolic BP (mmHg)	69.7±10.5	68.5±11.1	0.057

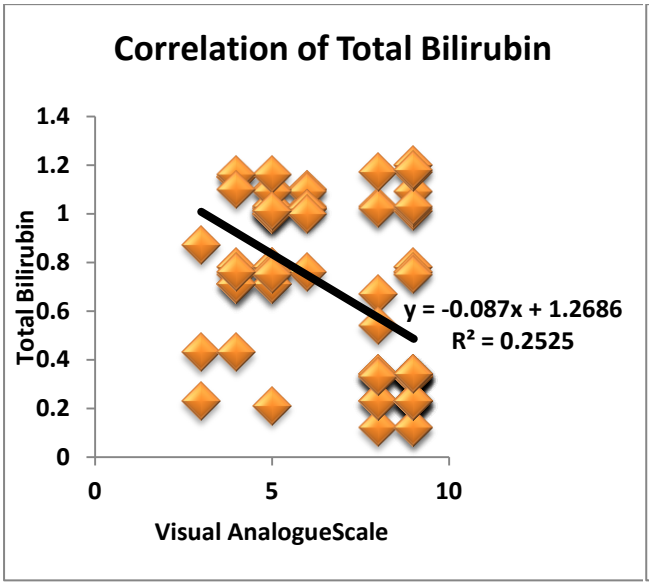
Table 2. Liver biomarkers in patient & control

	Patients	Control	P-value
Bilirubin (total)	1.01±0.32	1.35±0.07	0.0003
Bilirubin (direct)	0.61±0.02	0.77±0.08	0.0002
Bilirubin (indirect)	0.13±0.02	0.28±0.05	0.003
Alanine transferase	34.9±4.5	35.7±3.6	0.091
Alkaline phosphatase	89.4±13.2	91.6±11.5	0.098
γ- Glutamyl Transferase	77.6±9.3	35.3±5.07	0.0001

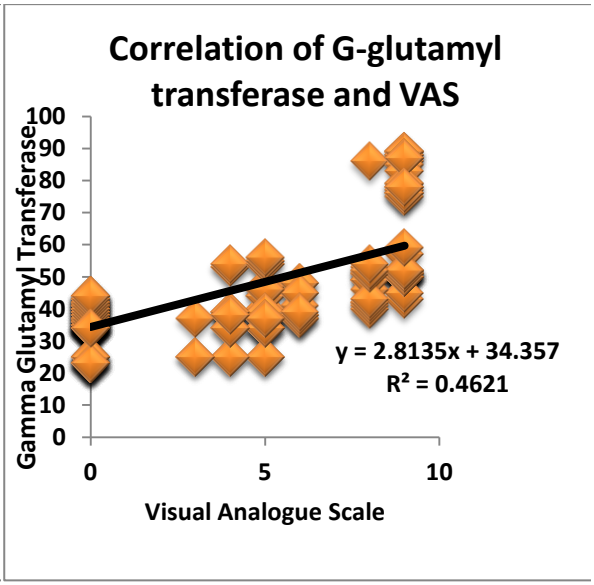
Table 3. Correlation of LFT and Migraine Pain Severity using Visual Analog Scale

	Bilirubin (total)	Bilirubin (Direct)	Bilirubin (Indirect)	Alanine transferse	Alkaline phosphatase	γ -GT
r-value	-0.753	-0.729	-0.453	0.021	0.069	0.871
p-value	<0.01	<0.01	<0.01	0.932	0.301	<0.01

r-value = correlation co-efficient, p-vlaue= level of significance



Graph 1. Negative correlation of total bilirubin and Visual Analogue Scale – migraine severity in migraine patients



Graph 2. Positive correlation of gamma glutamyl transferase and Visual Analogue Scale – migraine severity in migraine patients

DISCUSSION

The present prospective study analyzed the serum bilirubin and GGT in migraine diagnosed women and correlation with pain severity by VAS scale. Serum bilirubin was low and elevated GGT in migraine patients compared to controls (P<0.001). Study findings are in agreement with previous studies[11-15]. Elevated GGT is reported by few studies that is a new finding. Serum bilirubin (total, direct and Indirect) in patients and controls were found 1.01±0.32 vs. 1.35±0.07 mg/dl, 0.61±0.02 vs. 0.77±0.08 mg/dl, and 0.13±0.02 vs. 0.28±0.05 mg/dl respectively (P<0.003). GGT in migraine patients was 77.6±9.3 IU compared to 35.3±5.07 IU in controls this shows elevated GGT in migraine patients that is a new finding. Present study proves serum bilirubin may be used as clinical marker for migraine. Bilirubin is found elevated in diseases such as smokers, hypertension, & coronary artery diseases, etc.[11,12] A study[13] reported serum bilirubin may protect against atherosclerotic vascular diseases such as coronary artery disease. Other previous studies[14,15] reported negative correlation of bilirubin with vascular disease in obese, diabetic and smoker subjects and those suffering from metabolic syndrome. Our finding of low bilirubin in migraine is consistent with a previous study[15] that reported similar finding and concluded it may prove a clinical marker of neurogenic inflammation in migraine patients. This finding is consistent with above study. A previous study[14] analyzed 2784 sample and concluded low bilirubin in chronic kidney disease and potential risk factor for kidney function. The finding is in line with our present study as bilirubin has proved clinically significant marker in various diseases. Underlying mechanism of bilirubin is that acts as an anti – oxidant neutralizing free oxygen radical species (ROS).

The findings of present study are in line with prevoius studies[1,5-17] that have reported correlation of low bilirubin in atherosclerosis, ischemic heart disease, brain stroke and migraine. It is concluded that the low bilirubin is because of increased oxidative stress that consumed it resulting in low levels, this has been reported.[18,19] A previous study[20] reported neurogenic inflammation in migraine patients that increases pro–inflammatory cytokines stimulating nerve endings resulting in migraine. A previous study[21]concluded a low bilirubin level in migraine is because of increased oxidative stress of neurogenic inflammation. Present study is worth reporting on decreased serum bilirubin and elevated GGT in migraine. One limitation of present study is a small sample size; hence results cannot be generalized; however prospective design is worth enough for migraine patients.

CONCLUSION

The present study reveals low bilirubin levels and elevated gamma glutamyl transferase (GGT) in women suffering from migraine. Low bilirubin may prove clinical marker for neurogenic inflammation in migraine patients but this needs further research with large sample population.

ETHICS APPROVAL: The ERC gave ethical review approval. **ERC NO/:1786/2023/IU/675, DEC 2023.**

CONSENT TO PARTICIPATE: written and verbal consent was taken from subjects and next of kin.

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CONFLICT OF INTEREST: No competing interest declared.

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