L Inaotombi Devi
Department of Medical
Laboratory Technology,
Regional Institute of
Paramedical and Nursing Science
(RIPANS), Zemabawk, Aizawl,
Mizoram, India

Lalsanglura Ralte
Department of Medical
Laboratory Technology,
Regional Institute of
Paramedical and Nursing Science
(RIPANS), Zemabawk, Aizawl,
Mizoram, India

Lalnuntluangi Hmar
College of Veterinary Sciences &
A.H., Central Agricultural
University, Selesih, Aizawl,
Mizoram, India

M Ayub Ali
College of Veterinary Sciences &
A.H., Central Agricultural
University, Selesih, Aizawl,
Mizoram, India

Plasma biochemical profile of hepatocellular carcinoma patients

L Inaotombi Devi, Lalsanglura Ralte, Lalnuntluangi Hmar and M Ayub Ali

Abstract
Hepatocellular carcinoma (HCC) accounts for majority of the cases of primary liver cancer and is one of the most malignant tumors with a steadily increasing incidence worldwide. In HCC, the hepatic damage causes biochemical alterations in the body which are reflected in several tests. Assessment of these changes can be of value in the diagnosis. In the present investigation the plasma biochemical parameters including glucose, total cholesterol, triglycerides, HDL-C, total protein, albumin, globulin, A:G ratio, bilirubin (direct & total), creatinine, BUN, uric acid, calcium, phosphorus, magnesium, sodium, potassium, chloride, cholinesterase, SGOT, SGPT, alkaline phosphatase, CKMB and gamma glutamyl transferase of the HCC patients undergoing treatment were analyzed. The plasma levels of HDL-Cholesterol and Potassium were lower than the normal levels while the levels of Gamma Glutamyl Transferase, Aspartate transaminase, and Lactate Dehydrogenase were higher than the normal range.

Keywords: Hepatocellular carcinoma, HDL-cholesterol, potassium, GGT, LDH

Introduction
Cancer is a group of diseases involving abnormal cell growth with the potential to invade or spread to other parts of the body (WHO, 2018) [1]. The possible signs and symptoms of cancer include a lump, abnormal bleeding, prolonged cough, unexplained weight loss and a change in bowel movements. The causes of cancer are many which include infections, obesity, exposure to ionizing radiations etc. The use of tobacco is the cause of about 22% of cancer deaths. Another 10% are due to obesity, poor diet, lack of physical activity or excessive drinking of alcohol (WHO, 2018; NCI, 2012; Jayasekara *et al*., 2016) [1, 2, 3]. Other factors include certain infections, exposure to ionizing radiation and environmental pollutants (Anand *et al*., 2008) [4]. In developing countries, 15% of cancers are due to infections such as helicobacter pylori, hepatitis B, hepatitis C, human papilloma virus infection, Epstein-Barr virus and human immunodeficiency virus (HIV) (WHO, 2018) [1]. These factors act at least partly, by changing the genes of a cell. Typically, many genetic changes are required before cancer develops (WHO, 2014) [5]. Approximately 5-10% of cancers are due to inherited genetic defects from a person's parents (ACS, 2013) [6]. Many cancers can be prevented by not smoking, maintaining a healthy weight, not drinking too much alcohol, eating plenty of vegetables, fruits and whole grains, vaccination against certain infectious diseases, not eating too much processed red meat and avoiding too much sunlight exposure (Kushi *et al*., 2012; Parkin *et al*., 2011) [7, 8]. The most common types of cancer in males are lung cancer, prostate cancer, colorectal cancer and stomach cancer while in females, the most common types are breast cancer, colorectal cancer, lung cancer and cervical cancer (WHO, 2014) [5].

Liver cancer, also known as hepatic cancer and primary hepatic cancer, is cancer that starts in the liver. In most countries, hepatocellular carcinoma (HCC) accounts for majority (70-90%) of the cases of primary liver cancer (London and McGlynn, 2010) [9]. HCC is one of the most malignant tumors with a steadily increasing incidence worldwide (Venook *et al*., 2010) [10]. Risk factors for primary liver cancer include: having hepatitis B or C, heavy alcohol use, having cirrhosis or scarring of the liver, having hemochromatosis (an iron storage disease), obesity and diabetes. Most people don't have signs and symptoms in the early stages of HCC. When signs and symptoms of HCC appear, they may include general weakness and fatigue, abdominal pain or tenderness especially in the upper right part of the abdomen, swollen abdomen (ascites), nausea and vomiting, loss of appetite, unexplained weight loss, yellow skin or eyes (jaundice), light stools, and easy bruising or bleeding. The diagnosis of HCC is sometimes difficult and frequently requires various tests and procedures which include blood

Correspondence
M Ayub Ali
College of Veterinary Sciences &
A.H., Central Agricultural
University, Selesih, Aizawl,
Mizoram, India

tests, imaging tests, and removing a sample of liver tissue for testing. The most commonly used blood test for HCC is a tumor marker named alfa-fetoprotein (AFP). AFP levels greater than 400-500 ng/ml are considered diagnostic for HCC but less than half of patients have levels that high. The hepatic damage causes biochemical alterations in the body which are reflected in several tests. Assessment of these changes can be of value in the diagnosis. In HCC patients, HDL-fraction levels including HDL-phospholipids, HDL-cholesterol and the ratio of HDLC/HDL-PL are significantly lower (Ahaneku et al., 1992) [11]. Lower cholesterol level also results in poor prognosis in HCC patients (Jiang et al., 2016) [12]. Rasheed and Iqtidar (1995) [13] reported that serum potassium, bicarbonate, creatinine and uric acid levels raised while the serum sodium, chloride, urea, urea-nitrogen and residual nitrogen are reduced however these parameters showed improvement on treatment. In the present investigation, the blood plasma biochemical profile of the hepatocellular cancer patients undergoing treatment was evaluated.

Materials and Method
The present study was conducted with the established and histopathologically confirmed hepatocellular cancer patients being treated at Regional Cancer Hospital and Research Centre, Zemabawk, Aizawl, Mizoram. The blood samples (5 ml) each were collected from each patient aseptically in heparinized tubes. The samples were then centrifuged at 2500 g for 10 min and collected the plasma. The collected plasma samples were then analyzed for various biochemical parameters in a fully automatic dry clinical analyzer (Fujifilm-4000i). The observed results were then analyzed using a suitable statistical method as per Snedecor and Cochran (1994) [14].

Results and Discussions
The various blood plasma biochemical parameters including glucose, total cholesterol, triglycerides, HDL-Cholesterol, total protein, albumin, globulin, A:G ratio, bilirubin (direct & total), creatinine, BUN, uric acid, calcium, phosphorus, magnesium, sodium, potassium, chloride, cholinesterase, SGOT, SGPT, alkaline phosphatase, CKMB and gamma glutamyl transferase were analyzed. The observed blood plasma biochemical parameters in the present investigation is given n the Table 1.

Table 1: Plasma Biochemical profile of Hepatocellular cancer patients

Sl. No.	Test	Observed value	Normal Reference range
01	Glucose (mg/dl)	100.00±21.21	70-110 (Fasting) 110-150 (PP)
02	Cholesterol (mg/dl)	185.00±8.49	150-219
03	Triglyceride (mg/dl)	94.00±29.69	50-149
04	HDL-Cholesterol (mg/dl)	26.50±12.03	37-67 (Male) 40-71 (Female)
05	Total Protein (g/dl)	7.15±0.64	6.7-8.3
06	Albumin (g/dl)	4.00±0.14	3.8-5.0
07	Globulin (g/dl)	3.15±0.49	
08	A:G	1.28±0.15	
09	BUN (mg/dl)	9.30±2.68	8-23
10	Uric Acid (mg/dl)	6.1±0.71	4.0-7.0 (Male) 3.0-5.5 (Female)
11	Creatinine (mg/dl)	1.00±0.14	0.6-1.1
12	Bilirubin (Total) (mg/dl)	0.30±0.14	0.1-1.2
13	Bilirubin (Direct) (mg/dl)	0.10±0.00	0.1-0.4
14	Calcium (mg/dl)	8.55±0.64	8.4-10.2
15	Phosphorus (mg/dl)	3.55±0.64	2.6-4.4
16	Magnesium (mg/dl)	1.95±0.49	1.8-2.4
17	Sodium (mmol/L)	139.50±3.54	136-149
18	Potassium (mmol/L)	3.75±0.21	3.8-5.0
20	Chloride (mmol/L)	102.00±2.83	98-106
21	Alkaline Phosphatase (U/L)	109.50±16.26	32-111
22	Gamma Glutamyl Trannsferase (U/L)	136.00±28.28	16-73
23	Aspartate transaminase (U/L)	39.00±26.87	8-38
24	Alanine Transaminase (U/L)	16.50±4.94	4-44
25	CKMB (U/L)	16.00±12.73	<25
26	Lactate Dehydrogenase (U/L)	230.50±19.73	106-211

The plasma glucose level observed was 100.00±21.21 mg/dl. The observed level of total cholesterol, triglyceride and HDL-Cholesterol were respectively 185.00±8.49 mg/dl, 94.00±29.69 mg/dl and 26.50±12.03 mg/dl. The total cholesterol and triglyceride levels estimated were in the normal range while the level of HDL-Cholesterol estimated was lower than the normal level. The present finding of lower HDL-Cholesterol is in agreement with the findings of Ahaneku et al. (1992) [11] and Jiang et al. (2016) [12]. The decrease level of HDL-Cholesterol is because of the fact that in chronic liver diseases and HCC, the metabolism and synthesis of cholesterol are damaged which lead to a decrease in plasma cholesterol levels (Cooper et al., 1996; Ooi et al., 2005) [15, 16]. The decrease in the level of HDL-Cholesterol was also observed in breast cancer (Devi et al., 2015) [17], gastric cancer (Devi et al., 2016) [18] and cervical cancer (Devi et al., 2018) [19]. The total protein, albumin, globulin and A:G estimated were 7.15±0.64 g/dl, 4.00±0.14 g/dl, 3.15±0.49 g/dl and 1.28±0.15 respectively. The values observed are within the normal range. The observed BUN, Uric acid and Creatinine levels were 9.30±2.68 mg/dl, 6.10±0.71 mg/dl and 1.00±0.14 mg/dl respectively which is within the normal

range. The observed level of uric acid in present investigation is in contrast to finding reported by Rasheed and Iqtidar (1995) [13]. Rasheed and Iqtidar (1995) [13] reported a increase in the levels of uric acid in HCC patients. The level of Total Bilirubin and Direct Bilirubin observed were respectively 0.30±0.14 mg/dl and 0.10±0.00 mg/dl which are within the normal range in contrast to reports in literature. Nandennavar et al. (2017) [20] reported hyperbilirubinemia in 22 of the 53 HCC patients (41%). The observed normal levels of albumin, creatinine, uric acid and bilirubin in the present investigation may be because of the fact that these parameters were evaluated on the samples collected from the patients undergoing treatment. Rasheed and Iqtidar (1995) [13] reported that after 9-10 months treatment, patients showed improvement in these parameters. The observed levels of Calcium, Phosphorus, Magnesium, Sodium, Potassium and Chloride were 8.55±0.64 mg/dl, 3.55±0.64 mg/dl, 1.95±0.49 mg/dl, 139.50 mmol/L, 3.75±0.21 mmol/L and 102.00±2.83 mmol/L respectively. The value observed are within the normal range except for potassium which shows somewhat lower than the normal level. The observed lower level of plasma potassium is in agreement with the findings of Rasheed and Iqtidar (1995) [13].

The levels of plasma Alkaline phosphatase, Gamma Glutamyl Transferase (GGT), Aspartate transaminase, Alanine Transaminase, CKMB and Lactate Dehydrogenase were respectively 109.50±16.26 U/L, 136.00±28.28 U/L, 39.00±26.87 U/L, 16.50±4.94 U/L, 16.00±12.73 and 230.50±19.73 U/L. The levels of gamma glutamyltransferase, aspartate tranaminase and lactate dehydrogenase were on higher side and the level of alkaline phosphatase was on higher margin of the normal reference range. The raised level of gamma glutamyltransferase in also reported in gastric cancer patients and cervix cancer patients (Devi et al., 2016; Devi et al., 2018) [18, 19] while the increase level of alkaline phosphates is also observed among the breast cancer, gastric cancer and cervix cancer patients (Devi et al., 2015; Devi et al., 2016; Devi et al., 2018) [17, 18, 19]. The raised in the level of aspartate transaminase was also reported by Nandennavar et al. (2017) [20] in 26% of the hepatocellular cancer patients.

Acknowledgement

References

1. World Health Organization (WHO). Cancer, 2018. Retrieved 19 December 2018.
2. National Cancer Institute (NCI). Obesity and Cancer Risk, 2012. Archived from the original on 4 July 2015.
3. Jayasekara H, MacInnis RJ, Room R, English DR. Long-Term Alcohol Consumption and Breast, Upper Aero-Digestive Tract and Colorectal Cancer Risk: A Systematic Review and Meta-Analysis. Alcohol and Alcoholism. 2016; 51(3):315-330.
4. Anand P, Kunnumakkara AB, Sundaram C, Harikumar KB, Tharakan ST, Lai OS et al. Cancer is a preventable disease that requires major lifestyle changes. Pharmaceutical Research. 2008; 25(9):2097-2116.
5. World Health Organization (WHO). World Cancer Report. 2014. pp. Chapter 1.1. ISBN 978-92-832-0429-9. Archived from the original on 12 July 2017.
6. American Cancer Society (ACS). Heredity and Cancer. 2013. Archived from the original on 2 August 2013.
7. Kushi LH, Doyle C, McCullough M, Rock CL, Demark-Wahnefried W, Bandera EV et al. American Cancer Society Guidelines on nutrition and physical activity for cancer prevention: reducing the risk of cancer with healthy food choices and physical activity. CA Cancer J Clin. 2012; 62(1):30-67.
8. Parkin DM, Boyd L, Walker LC. The fraction of cancer attributable to lifestyle and environmental factors in the UK in 2010". British Journal of Cancer. 2011; 105(Suppl 2):77-81.
9. London WT, McGlynn KA. Liver cancer. In: Schottenfeld D, Fraumeni J Jr, eds. Cancer Epidemiology and Prevention. 3rd ed. New York: Oxford University Press. 2006:763-786.
10. Venook AP, Papandreaou P, Furusi J, Ladran de, Guevara L. The incidence and epidemiology of hepatocellular carcinoma: A global and regional perspective. The Oncologist. 2010; 15:5-13.
11. Ahaneku JE, Taylor GO, Olubuyide IO, Agbedana EO. Abnormal lipid and lipoprotein patterns in liver cirrhosis with and without hepatocellular carcinoma. JPMA The Journal of the Pakistan Medical Association. 1992; 42:260-263.
12. Jiang SS, Weng DS, Jiang L, Zhang YJ, Pan K, Pan QZ, et al. The clinical significance of preoperative serum cholesterol and high-density lipoprotein-cholesterol levels in hepatocellular carcinoma. Journal of cancer. 2016; 7:626-632.
13. Rasheed A, Iqtidar A. Biochemical profile in liver cancer patients. 1995; 16(4):366-367.
14. Snedecor GW, Cochran WG. Statistical Method. 8th Edn. Oxford and IBH Publishing Co., New Delhi. 1989
15. Cooper ME, Akdeniz A, Hardy KJ. Effects of liver transplantation and resection on lipid parameters: a longitudinal study. The Australian and New Zealand journal of surgery. 1996; 66:743-746.
16. Ooi K, Shiraki K, Sakurai Y, Morishita Y, Nobori T. Clinical significance of abnormal lipoprotein patterns in liver diseases. International journal of molecular medicine. 2005; 15:655-660.
17. Devi LI, Ralte L, Ali MA. Serum biochemical profile of breast cancer patients. European Journal of Pharmaceutical and Medical Research. 2015; 2(6):210-214.
18. Devi LI, Ralte L, Ali MA. Serum biochemical profile of gastric cancer patients. European Journal of Pharmaceutical and Medical Research. 2016; 3(5):431-434.
19. Devi LI, Ralte L, Hmar L, Ali MA. Serum biochemical profile of patients suffering from cervical cancer in Mizoram. International Journal of Chemical Studies. 2018; 6(6):883-886.
20. Nandennavar MI, Karpurmath SV, Mandakalatur G, Prasad AE. Clinical profile of hepatocellular carcinoma and experience with sorafenib from a tertiary cancer centre in Southern India. International J. of Research in Medical Sciences. 2017; 5(2):379-383.