

COMPARISON OF SERUM ALANINE AMINOTRANSFERASE (ALT) OF NEWLY DIAGNOSED PATIENTS OF HEPATITIS C WITH HEALTHY INDIVIDUALS

*MUHAMMAD HUMAYUN , **ZAMEER AHAMAD,***MUHAMMAD MUSTANSAR, ****AMBREEN KHALID

**ASSISTANT PROFESSOR BIOCHEMISTRY .SHALAMAR MEDICAL AND DENTAL COLLEGE LAHORE*

***PROF. OF BIOCHEMISTRY AND PRINCIPAL. SAHIWAL MEDICAL COLLEGE SAHIWAL*

****ASSISTANT PROFESSOR BIOCHEMISTRY. SAHIWAL MEDICAL COLLEGE SAHIWAL*

*****ASSISTANT PROFESSOR PHYSIOLOGY. SHALMAR MEDICAL AND DENTAL COLLEGE LAHORE*

CORRESPONDENCE TO DR. MUHAMMAD HUMAYUN, ASSISTANT PROFESSOR EMAIL: MRHUMAYUNDR@GMAIL.COM

ABSTRACT

VIRAL HEPATITIS IS ONE OF THE MAJOR PUBLIC HEALTH PROBLEM ALL OVER THE WORLD. ONCE INFECTION WITH HCV OCCURS IT LEADS TO CHRONICITY IN UPTO 85% OF CASES. THIS CAN LEAD TO CIRRHOSIS, HEPATOCELLULAR CARCINOMA AND LIVER FAILURE. THE SERUM ALANINE AMINOTRANSFERASE (ALT) LEVEL TEST HAD BEEN SHOWN TO BE A VIABLE AND COST-EFFECTIVE SCREENING TEST FOR HCV INFECTION THAT COULD REDUCE THE INCIDENCE OF POST-TRANSFUSION INFECTION. SERUM ALANINE AMINO TRANSFERASE (ALT) IS THE MOST FREQUENTLY UTILIZED SCREENING TEST IN ROUTINE EVALUATION OF LIVER DAMAGE. DONORS WITH INCREASED CATALYTIC ACTIVITY OF ALT ARE EXCLUDED FROM FUTURE BLOOD DONATIONS, EVEN IF THEIR ANTI HEPATITIS C VIRUS STATUS IS NON REACTIVE. PRESENT STUDY WAS TO EVALUATE THE IMPORTANCE OF S/ALT IN NEWLY DIAGNOSED PATIENTS OF HCV FROM THE BLOOD DONORS AND THE COMPARISON WITH NORMAL HEALTHY INDIVIDUALS WITH SERONEGATIVE HCV WITH SAME RATIO OF AGE, SEX AND BMI . IN THE PRESENT STUDY 100 PATIENTS NEWLY DIAGNOSED PATIENTS OF HCV WERE ENROLLED, COMPARED WITH 100 NORMAL HEALTHY INDIVIDUALS. THE MEAN S/ALT IN NORMAL PERSONS WAS 25.22 ± 8.03 AND IN NEWLY DIAGNOSED PATIENTS WAS 48.75 ± 6.26 WITH P VALUE 0.035 WHICH IS SIGNIFICANT.: FROM OUR STUDY WE CAN CONCLUDED THAT S/ALT CAN BE A USEFUL MARKER FOR THE DIAGNOSIS OF HCV IN BLOOD DONORS AND IN WHOM THERE IS SOME TECHNICAL PROBLEM TO DIAGNOSE BY ROUTINE SCREENING TEST.

KEY WORDS: HEPATITIS, S/ALT, BMI

INTRODUCTION

VIRAL HEPATITIS IS ONE OF THE MAJOR PUBLIC HEALTH PROBLEM ALL OVER THE WORLD. ONCE INFECTION WITH HCV OCCURS IT LEADS TO CHRONICITY IN UPTO 85% OF CASES¹. THERE ARE ABOUT 170 MILLION PEOPLE INFECTED CHRONICALLY WITH HCV². UP TO 70 % OF CHRONICALLY INFECTED INDIVIDUAL DEVELOP ACTIVE LIVER DISEASE³. THIS CAN LEAD TO CIRRHOSIS, HEPATOCELLULAR CARCINOMA AND LIVER FALIUER⁴. ANTIBODY TO HCV (ANTI-HCV) TEST IS THE ACCEPTED METHOD FOR THE DIAGNOSIS OF HCV INFECTION. IT IS ROUTINELY USED IN THE SCREENING FOR HCV INFECTION AMONG BLOOD DONORS. THE SERUM ALANINE AMINOTRANSFERASE (ALT) LEVEL TEST HAD BEEN SHOWN TO BE A VIABLE AND COST-EFFECTIVE SCREENING TEST FOR HCV INFECTION THAT COULD REDUCE THE INCIDENCE OF POSTTRANSFUSION INFECTION^{5,6}. SERUM ALANINE AMINO TRANSFERASE (ALT) IS THE MOST FREQUENTLY UTILIZED SCREENING TEST IN ROUTINE EVALUATION OF LIVER DAMAGE⁷. DONORS WITH INCREASED CATALYTIC ACTIVITY OF ALT ARE EXCLUDED FROM FUTURE BLOOD DONATIONS, EVEN IF THEIR ANTI HEPATITIS C VIRUS STATUS IS NON REACTIVE⁸. IT IS EXPECTED THAT A NUMBER OF ASYMPTOMATIC DONORS WOULD BE SUFFERING FROM EARLY HEPATITIS C AT THE TIME OF BLOOD DONATION. FAILURE TO DIAGNOSE EARLY INFECTION MAY BE SECONDARY TO UNDETECTABLE LEVELS OF HEPATITIS C VIRUS ANTIBODIES DURING INITIAL PHASE OF INFECTION. THIS IS FURTHER COMPOUNDED BY DIFFERENT SENSITIVITIES AND SPECIFICITIES OF VARIOUS COMMERCIALY AVAILABLE REAGENTS WHICH ARE BEING USED FOR DETECTION OF ANTI-HCV⁹. POLYMERASE CHAIN REACTION WHICH CAN BE SUCCESSFULLY EMPLOYED FOR RECOGNITION OF HEPATITIS C VIRUS RIBONUCLEIC ACID IS NEITHER PRACTICAL NOR COST EFFECTIVE FOR DEVELOPING COUNTRIES. BECAUSE OF THESE OBSTACLES, ALT TESTING MAY SERVE AS A PROBABLE INDICATOR OF CONTINUOUS VIRAL

REPLICATION REFLECTING A POSSIBLE CHRONIC HEPATIC INVOLVEMENT AS WELL AS POTENTIAL INFECTIVITY¹⁰. ALANINE AMINOTRANSFERASE (ALT), A SENSITIVE INDICATOR OF LIVER CELL INJURY, HAS BEEN USED TO IDENTIFY PATIENTS WITH LIVER DISEASE FOR ALMOST 50 YEARS¹¹. THIS CYTOSOLIC ENZYME, WHICH IS FOUND IN MANY ORGANS, CATALYZES THE TRANSFER OF THE AMINO GROUP FROM ALANINE TO α -KETOGlutARIC ACID¹².

ALANINE AMINOTRANSFERASE LEVELS ARE PARTICULARLY HIGH IN THE LIVER. FOR DETECTION OF LIVER DISEASES, ALT IS THOUGHT TO BE A MORE SPECIFIC INDICATOR THAN ASPARTATE AMINOTRANSFERASE, AN ENZYME FOUND IN CYTOSOL AND MITOCHONDRIA. SERUM LEVELS OF ALT NORMALLY ARE LOW 10 TO 40 U/L IN MOST LABORATORIES; HOWEVER, NORMAL VALUES MAY VARY GREATLY AMONG LABORATORIES. ELEVATED SERUM ALT LEVELS HELP IDENTIFY MANY TYPES OF LIVER DISEASES IN PATIENTS AND WERE WIDELY USED IN THE 1980S TO SCREEN BLOOD DONORS FOR NON-A, NON-B HEPATITIS¹³.

ANY TYPE OF LIVER CELL INJURY CAN MODESTLY INCREASE ALT LEVELS. MARKED ELEVATIONS THAT IS, ALT LEVELS GREATER THAN 500 U/L OCCUR MOST OFTEN IN PERSONS WITH DISEASES THAT AFFECT PRIMARILY HEPATOCYTES, SUCH AS VIRAL HEPATITIS, ISCHEMIC LIVER INJURY (SHOCK LIVER), AND TOXIN-INDUCED LIVER DAMAGE. DESPITE THE ASSOCIATION BETWEEN GREATLY ELEVATED ALT LEVELS AND HEPATOCELLULAR DISEASES, THE ABSOLUTE HEIGHT OF THE ALT ELEVATION DOES NOT CORRELATE WITH THE EXTENT OF LIVER CELL DAMAGE. CURRENTLY, MEASUREMENT OF SERUM ALT LEVELS IS THE MOST FREQUENTLY USED TEST TO IDENTIFY PATIENTS WITH LIVER DISEASES¹⁴. KHOURI ST ET-AL SUGGEST THAT ALT CAN BE A USEFUL MARKER FOR DETECTION OF HEPATITIS C VIRUS INFECTED DONORS IN WHOM TECHNICAL PROBLEMS MIGHT HAVE OCCURRED IN SEROLOGICAL SCREENING¹⁵. TRANSAMINASES ARE WIDELY DISTRIBUTED THROUGHOUT THE BODY. AST IS FOUND PRIMARILY IN THE HEART, LIVER SKELETAL MUSCLE AND KIDNEY, WHERE AS ALT IS FOUND PRIMARILY IN THE LIVER AND KIDNEY, WITH LESS AMOUNT IN HEART AND SKELETAL MUSCLE. ALT IS EXCLUSIVELY CYTOPLASMIC, BOTH CYTOPLASMIC AND MITOCHONDRIAL FORMS OF AST ARE FOUND IN CELLS. THESE ARE GENETICALLY DISTINCT ISOENZYMES WITH A DIMERIC STRUCTURE COMPOSED OF TWO IDENTICAL POLYPEPTIDE SUBUNIT OF ABOUT 400 AMINOACIDS RESIDUES¹⁶. PERSISTENCE OF INCREASED ALT FOR MORE THAN 6 MONTHS AFTER AN EPISODE OF ACUTE HEPATITIS IS USED TO DIAGNOSE CHRONIC HEPATITIS. MOST PATIENTS WITH CHRONIC HEPATITIS HAVE MAXIMUM ALT LESS THAN SEVEN TIMES THE UPPER REFERENCE LIMIT. ALT MAY BE PERSISTENTLY A NORMAL IN 15% - 50% OF PATIENTS WITH CHRONIC HEPATITIS C. IN PATIENTS WITH ACUTE HEPATITIS C, ALT SHOULD BE MEASURED PERIODICALLY OVER 1-2 YEARS TO DETERMINE IF IT BECOME AND STAY NORMAL¹⁷.

AIMS AND OBJECTIVES

TO EVALUATE THE IMPORTANCE OF ALT FOR THE DIAGNOSIS OF HCV INFECTION AND TO DETERMINE THE AFFECT OF HCV ON LIVER CELLS IN EARLY STAGES. THE STUDY AIMS TO CORRELATE THE ASSOCIATION OF HEPATITIS C VIRUS RIBONUCLEIC ACID WITH SERUM ALANINE TRANSAMINASE IN HEALTHY SERONEGATIVE BLOOD DONORS

MATERIALS AND METHODS

A TOTAL 100 BLOOD DONORS WITH HCV POSITIVE WERE ENROLLED FROM THE BLOOD BANKS OF MAYO HOSPITAL, SERVICES HOSPITAL, GANGA RAM HOSPITAL AND JINNAH HOSPITAL. THESE PATIENTS WERE ACCIDENTALLY DIAGNOSED HAVING HCV INFECTION BY DOT IMMUNO-CHROMATOGRAPHIC METHOD USING NOBIS ANTI HCV

COMMERCIAL KIT. BLOOD SAMPLES WERE COLLECTED FOR ESTIMATION OF SERUM ALT LEVEL. 2 CC BLOOD SAMPLE COLLECTED ASEPTICALLY SERUM SEPARATED BY CENTRIFUGATION AND SHIFTED TO LABORATORY FOR ESTIMATION SERUM ALT BY KINETIC METHOD WITH SPECTROPHOTOMETER AT A REACTION WAVELENGTH OF 340 NANOMETER AT A TEMPERATURE OF 25°C. ALT LEVELS OF ALL DIAGNOSED WERE EVALUATED WITH RESPECT TO AGE, BMI AND GENDER AND ALSO OF NORMAL HEALTHY SUBJECTS. REFERENCE RANGE IN THE LAB WAS 5-30 U/L. MARKEDLY ELEVATED ALT WAS DEFINED AS RESULTS GREATER THAN TWICE THE UPPER LIMIT OF REFERENCE RANGE. BASIC DESCRIPTIVE STATISTIC WERE PERFORMED USING SPSS-10

RESULTS

IN THE PRESENT STUDY 100 PATIENTS WERE ENROLLED WITH THE MEAN AGE 27.78 ± 5.29 YEARS AND 100 NORMAL HEALTHY INDIVIDUALS WITH MEAN AGE 24.63 ± 4.49 YEARS AND P VALUE IS 4.9 WHICH IS NOT SIGNIFICANT (TABLE 1). IN NORMAL INDIVIDUALS 74 WERE MALES AND 26 WERE FEMALES AND IN HCV POSITIVE PATIENTS 81 WERE MALES AND 19 WERE FEMALES (TABLE 2). MEAN BMI OF HCV NEGATIVE INDIVIDUALS WAS 27.99 ± 1.92 KG/M² AND THAT OF HCV POSITIVE WAS 28.44 ± 2.08 AND P VALUE IS 0.0573 WHICH IS ALSO NOT SIGNIFICANT (TABLE 3). THE MEAN S/ALT LEVEL WAS 25.55 ± 8.03 IU FOR NORMAL HEALTHY INDIVIDUALS AND FOR HCV POSITIVE PATIENTS IT WAS 48.75 ± 6.26 AND P VALUE IS 0.035 WHICH IS LESS THAN 0.05 AND IS SIGNIFICANT (TABLE 4).

Table 1: Comparison of age in years between HCV positive and normal individual

Status	mean	SD	P Value
HCV navigate (n=100)	24.63	4.49	4.9
HCV positive (n=100)	27.78	5.29	

Table.2 Sex distribution between HCV positive and normal individuals

Status	Male	Female
HCV navigate (n=100)	74	26
HCV Positive (n=100)	81	19

Table.3: Comparison of body mass index between HCV positive and normal individuals

Status	Mean	SD	P Vaule
HCV navigate (n=100)	27.99	1.92	0.0573
HCV Positive n=100	28.44	2.08	

Table.4: Comparison of Serum ALT levels between HCV positive and normal healthy individuals

Status	Mean	SD	P Value
HCV navigate (n=100)	25.55	8.03	0.035
HCV Positive (n=100)	48.75	6.26	

DISCUSSION

VIRAL HEPATITIS IS ONE OF THE MAJOR PUBLIC HEALTH PROBLEM ALL OVER THE WORLD. ONCE INFECTION WITH HCV OCCURS IT LEADS TO CHRONICITY IN UPTO 85% OF CASES¹. THE SERUM ALANINE AMINOTRANSFERASE (ALT) LEVEL TEST HAD BEEN SHOWN TO BE A VIABLE AND COST-EFFECTIVE SCREENING TEST FOR HCV INFECTION THAT COULD REDUCE THE INCIDENCE OF POSTTRANSFUSION INFECTION^{5,6}. SERUM ALANINE AMINO TRANSFERASE (ALT) IS THE MOST FREQUENTLY UTILIZED SCREENING TEST IN ROUTINE EVALUATION OF LIVER DAMAGE⁷. DONORS WITH INCREASED CATALYTIC ACTIVITY OF ALT ARE EXCLUDED FROM FUTURE BLOOD DONATIONS, EVEN IF THEIR ANTI HEPATITIS C VIRUS STATUS IS NON REACTIVE⁸.

PRESENT STUDY WAS TO EVALUATE THE IMPORTANCE OF S/ALT IN NEWLY DIAGNOSED PATIENTS OF HCV FROM THE BLOOD DINERS AND THE COMPARISON WITH NORMAL HEALTHY INDIVIDUALS WITH SERONEGATIVE HCV WITH SAME RATIO OF AGE, SEX AND BMI. SO THERE IS NO SIGNIFICANT DIFFERENCE BETWEEN THE TWO GROUPS REGARDING TO AGE, SEX AND BMI AS P VALUE IS NOT LESS THAN 0.05 AS SHOWN IN TABLES. THE MEAN S/ALT IN NORMAL PERSONS WAS 25.22 ± 8.03 AND IN NEWLY DIAGNOSED PATIENTS WAS 48.75 ± 6.26 WITH P VALUE 0.035 WHICH IS SIGNIFICANT. THIS SUGGEST THAT THE S/ALT LEVEL CAN BE GOOD MARKER TO DIAGNOSED HCV IN WHOM THERE IS SOME TECHNICAL PROBLEM OF THE DETECTION OF HCV IN ROUTINE SCREENING METHODS. DR. C. K. LIN ET-AL ALSO SUGGEST THAT THERE IS A DIRECT RELATION SHIP BETWEEN SERUM ALT AND ANTI-HCV POSITIVITY AND THERE IS DIRECT CORRELATION BETWEEN SERUM LEVEL AND ANTI-HCV RATIO¹⁸. OUR STUDY IS SUPPORTED BY KHOURI ST ET-AL WHO NARRATED THAT ALT CAN BE A USEFUL MARKER FOR THE DETECTION OF HCV INFECTED DONORS IN WHOM TECHNICAL PROBLEMS MIGHT HAVE OCCURRED IN SEROLOGICAL SCREENING¹⁹. HOWEVER SAAB S ET-AL CONCLUDED AGAINST OUR RESULTS, ACCORDING TO HIM A NEWLY ELEVATED AMINOTRANSFERASE LEVEL WAS NEITHER SENSITIVE NOR POSITIVELY PREDICTIVE OF CHRONIC INFECTION.

THEREFORE, AN ELEVATED ALT LEVEL IS AN INEFFECTIVE METHOD FOR SCREENING FOR HCV INFECTION IN HEMODIALYSED PATIENTS²⁰.

CONCLUSION

FROM OUR STUDY WE CAN CONCLUDED THAT S/ALT CAN BE A USEFUL MARKER FOR THE DIAGNOSIS OF HCV IN BLOOD DONORS AND IN WHOM THERE IS SOME TECHNICAL PROBLEM TO DIAGNOSE BY ROUTINE SCREENING TEST.

REFERENCES

1. PERLMAN BL. HEPATITIS C INFECTION : A CLINICALREVIEW. SOUTH MED J 2004; 97 (4):364-73
2. WHO GLOBAL SURVEILLANCE AND CONTROL OF HEPATITIS C: REPORT OF A WHO CONSOLTATION ORGANIZED IN COLLABORATION WITH THE VIRAL HEPATITIS PREVENTION BOARD , ANTWERP.BELGIUM. J VIRAL HEPAT 1999;6:35-47
3. CORNY-CANTILENA C, VANRADEN M, GIBBLE J, MELPOLDER J, SHAKIL AO, VILADOMIU L ET AL . ROUTS OF INFECTION, VIREMIA AND LIVER DISEASE IN BLOOD DONORS FOUND TO HAVE HEPATITIS C VIRUS INFECTION. N ENGL J MED 1996;334:1691-6.
4. ZEIN NN. THE EPIDEMIOLOGY AND NATURAL HISTORY OF HEPATITIS C VIRUS INFECTION. CLEVE CLIN J MED 2003;70 (SUPPL 4):S2-6
5. FRIEDMAN LS, DIENSTAG JL, WATKINS E, ET AL. EVALUATION OF BLOOD DONORS WITH ELEVATED SERUM ALANINE AMINOTRANSFERASE LEVELS. ANN INTERN MED. 1987;107:137-144.
6. AACH RD, SZMUNESS W, MOSLEY JW, ET AL. SERUM ALANINE AMINOTRANSFERASE OF DONORS IN RELATION TO THE RISK OF NON-A, NON-B HEPATITIS IN RECIPIENTS: THE TRANSFUSIONTRANSMITTED VIRUSES STUDY. N ENGL J MED. 1981;304:989-994..
7. OZER J, RATNER M, SHAW M, BAILEY W, SCHOMAKER S. THE CURRENT STATE OF SERUM BIOMARKERS OF HEPATOTOXICITY. TOXICOLOGY 2008;245:194-
8. KHOKHAR N, GILL ML, MALIK GJ. GENERAL SEROPREVALENCE OF HEPATITIS C AND HEPATITIS B VIRUS INFECTIONS IN POPULATION. J COLL PHYSICIANS SURG PAK 2004;14:534-
9. GRETCH DR. USE AND INTERPRETATION OF HCV DIAGNOSTIC TESTS IN THE CLINICAL SETTING. CLIN LIVER DIS 1997;1:543.
10. ALI SA, DONAHUE RM, QURESHI H, HEPATITIS B AND HEPATITIS C IN PAKISTAN: PREVALENCE AND RISK FACTORS. INT J INFECT Dis 2009;13:9-19. 1955; 34:126-33.
11. AWAPARA J, SEALE B. DISTRIBUTION OF TRANSAMINASES IN RAT ORGANS. J BIOL CHEM. 1952;194:497-502.
12. REJ R. ASPARTATE AMINOTRANSFERASE ACTIVITY AND ISOENZYME PROPORTIONS IN HUMAN LIVER TISSUES. CLIN CHEM. 1971;24:24-9.
13. KALLEI L, HAHN A, RODER VZ. CORRELATION BETWEEN HISTOLOGICAL FINDINGS AND SERUM TRANSAMINASE VALUES IN CHRONIC DISEASES OF THE LIVER. ACTA MEDICA SCANDINAVIKA. 1964;175:49-56.
14. KHOURI ST, LOPES EP, PEREZ RM, FIGUEIREDO VM, LANZONI VP, SILVA AE. LAB. DETERMINATION OF ALANINE AMINOTRANSFERASE IN BLOOD DONOR SCREENING--EVIDENCE OF ITS USEFULNESS IN THE PREVENTION OF POST-TRANSFUSION HEPATITIS 2004;50 (5-6):291-4.
15. PENTEGINI M. ASPARTATE AMINOTRANSFERASE ISOENZYME. CLIN BIOCHEM 1990;23:311-9
16. DUFOUR DR , LOTT JA, NOLTR FS, GRETCH DR , KOFF RS, SEEFF LB. DIAGNOSIS AND MONITORING OF HEPATIC INJURY.
17. II) RECOMMENDATIONS FOR USE OF LABORATORY TEST IN SCREENING, DIAGNOSIS AND MONITORING . CLIN CHEM. 2000;46:2050 – 68
18. DR.C.K. LIN, R.CHU, K.B.LI, S. LEONG , VOX SANGUINIS – VOLUME 62 , ISSUE 2 ,98 -101 MARCH 1992
19. khouri ST, Lopes EP, perez RM ,Figueiredo VM, Lanzoni VP, Silva AE and Ferraz ML . determination of alanine aminotransferase in blood donor screening – evidance of ite usefulness in prevention of post—tranfustion hepatitis --- Cli Lab. 2004;50(5-6):291-4
20. Saab S, Martin P , brezina M, Gintinic G, Yee HF Jr. Serum alanine aminotransferase in hepatitis C screeninig of patients on hemodialysis Am J Kidney Dis. 2001 Feb; 37 (2): 308-15.