ISSN: 0975 -8542

Journal of Global Pharma Technology

Available Online at: www.jgpt.co.in

RESEARCH ARTICLE

# The Impact of Extraintistinal amobiosis on TP53 Gene in Patients with Hepatocellular Carcinoma

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## Abstract

In this study, 20 serum samples and 8 liver abscess biopsy specimens were taken from 20 hepatocellular carcinoma and *E. histolytica* infected patients**.** Laboratory findings of patients with liver abscess showed increased total white blood cell count (WBC), increased C-reactive protein, (AST), (ALT), alkaline phosphatase (ALP), gamma-glutamyl transpeptidase (GGT) and bilirubin. The result of PCR performed on liver abscess patients was positive for the DNA of *E.histolytica* infected patients and 8 biopsy liver abscess patients. To detect *TP 53 gene* in hepatocellular with liver abscess of all 8(100%), mutation occurred in sequences of TP53, and there were changes in several locations on the exons**.** Nucleotides changes were shown in TP53 gene Exon 147,152,160.203 and 235amplified from tumor liver cancer samples. The mutation occurred on nucleotides TCC, GGT, ACT, CGC and ATC of TP53 gene.

**Keywords:** *Extra intestinal amebiasis. TP53 gene, Hepatocellular carcinoma.*

## Introduction

Amoebiasis is an infectious disease caused by the intestinal protozoan Entamoeba *histolytica* which is transmitted oro-fecally and is correlated with poor hygienic conditions [1].It is estimated that (10%) of the population in the world is infected with *Entamoeba histolytica*, and (90%) of the infected individuals have no symptoms. It is probably the second most common cause of parasitic death worldwide [1].It was reported that approximately (10%) of world population and (50%) of developing countries population may be infected with this parasite. The infection is common even in developed countries, and nearly 1% of the American people are infected [2].

Although most of the infected people (80=99%) are asymptomatic, invasive amoebiasis causes disabling disease in about (50) million patients and causes 50,000 deaths per year, especially in the tropical belt of Asia, Latin America and Africa. After malaria and schistosomiasis, it is reported to be the third major parasitic mortality cause [3].The most common extra-intestinal complication of amoebiasis is hepatic. The parasite multiplies and lodges in only a small proportion of liver although trophozoites reach there in most amoebic dysentery cases.

Hepatic complications develop in about (2-10%) people infected with *E. histolytica* in the tropical areas [4].Many patients with amoebic colitis show enlarged tender livers without remarkable liver function abnormalities or fevers. This acute liver involvement (amoebic hepatitis) could be attributed to recurrent amoebic invasions from active colonic infections or to toxic colonic agents that reach the liver. Hepatic damage may not be caused by direct amebic infection, but by cytokines secreted from inflammatory cells around trophozoites or lysosomal enzymes [5].Amebic hepatic abscesses most frequently develop in the age group (20-45) years.

The majority of patients present with acute disease, and the symptoms usually last for less than two weeks. The clinical signs and symptoms involve low-grade fever, chills, abdominal pain, tenderness as well as hepatomegaly.

Left lobe abscess usually present with toxemia, tenderness, epigastric pain and big epigastric masses. Multiple liver abscesses often present with toxemia, high fever, jaundice and encephalopathy. Secondary bacterial infections, ruptures and bile duct compressions are usually the complications of liver abscess amebiasis [6].

Hepatic complications develop in about (2-10%) people infected with *E. histolytica* in the tropical areas [7]. This case indicates an unusual initial HCC appearing as a hepatic abscess in a formerly healthy woman suffering from nonalcoholic fatty hepatic disease without cirrhosis [8].Abscess-like clinical features may be seen in HCC due to neoplasm-associated granulocytosis. Fever results from pyrogen production by macrophages or by malignant tumor cells, making HCC to be difficult to be distinguished from liver abscesses [8].

## Martial and Mothers

In the current study, 20 serum samples and 8 liver abscess biopsy specimens were taken from 20 hepatocellular carcinoma and *E. histolytica* infected patients who attended to Al-Barra mean lab during the period from 3rd may 2018 to 1st April 2019. Commercially available ELISA kit was used to detect *Entamoeba* antigens which are less expensive and more easily performed and are being used with increasing frequency and it is of greater sensitivity than microscopy to detect *E. histiolytica* specifically. Laboratory biopsy examination was performed to detect hepatic cancer and liver abscesses amobeosis complications as well as performing the hematological and biochemical tests. The mutation analysis was done by PCR, and the synonymous mutations were analyzed for codon usage. The primer used was 5′-ATGGAACCAGACAGAAAAGC-3′; F: 5′-GCTACTTGTTCTTGAGTGAAG-3′.DNA isolation. Tumor areas in the hepatic specimens were localized by histological examination of tissue sections stained with hematoxylin and eosin dyes. Results obtained from this study and data from Bali and Bebokwere (2016) [9] were analyzed to predict the amino acid changes by the computer program MEGA version 2.1 (Hu, *et al* ,2016), [10].

## Statistical Analysis

SPSS Vr.24 program and t-test were used for statistical analysis of the data.

## Results

The most common abnormalities of laboratory findings in patients with liver abscesses were elevated white blood cell count (WBC), C-reactive protein, (AST), (ALT), alkaline phosphatase (ALP), gamma-glutamyl transpeptidase (GGT) and bilirubin as shown in Table (1).

**Table 1: The abnormal parameters found in patients with amoebiasis in liver abscesses**

| Findings | % |
|---|---|
| C-reactive protein | 100% |
| Hemoglobin | 80% |
| Bilirubin | 70% |
| WBC | 80% |
| | |
| ALT | 75% |
| AST | 78% |
| ALP | 65% |
| GGT | 70% |
| Albumin | 77% |

The result of PCR performed on 8 biopsy samples of patients with liver abscess was positive for *E.* DNA. To detect *TP 53 gene* in hepatocellular with liver abscess pus of all 8(100%).

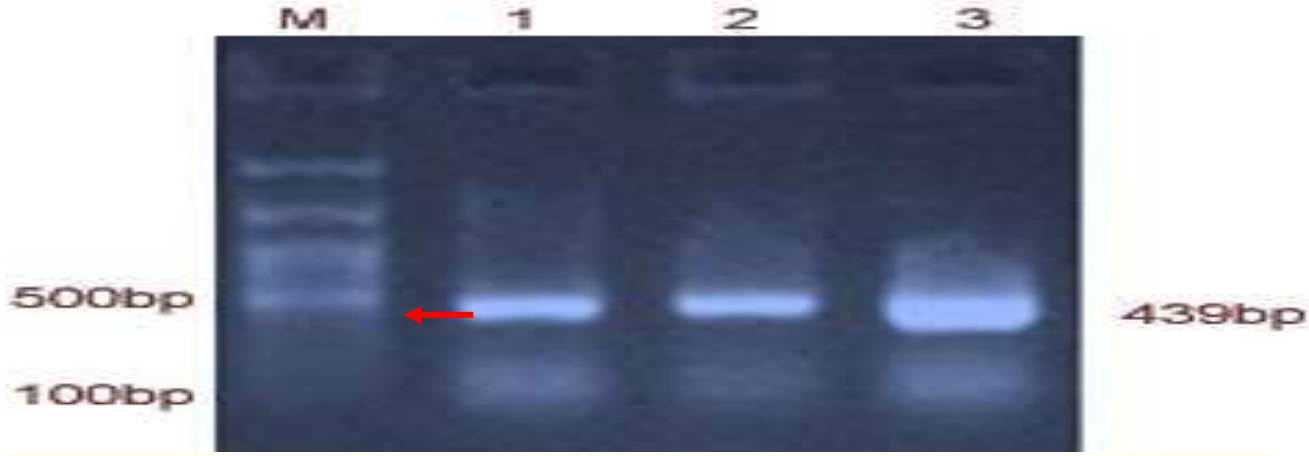


**Figure 1: The internal amplification control band is 439 bp respectively. Lane-1, 2 and 3, the M, 100 bp DNA ladder**

Mutation occurred in sequences of TP53 along with changes in several locations on the exons below as illustrated in Figure (2).

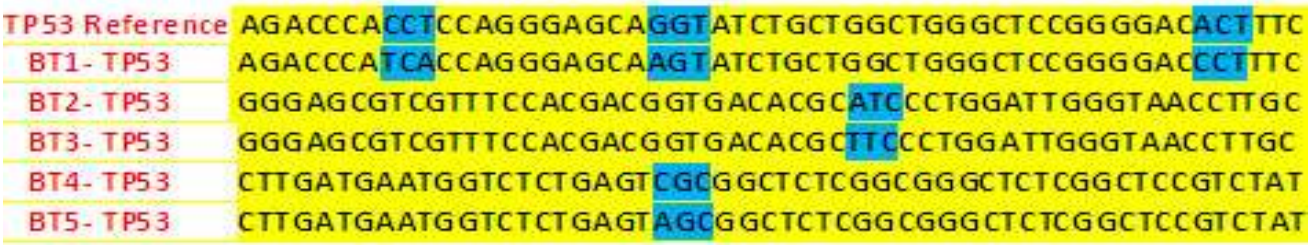


**Figure 2: The sequence of TP53 gene: Nucleotides changes shown in TP53 gene Exon 147,152,160.203 and 235amplified from tumor liver cancer samples. The mutation occurred on nucleotides TCC, GGT, ACT, CGC and ATC of TP53 gene**

**Table 2: Change obtained from hepatic cancer patients with liver abscess cysts infections, mutations were found in 6 out of 8 samples in numbers of exons in different position of TP53 gene**

| Specimen | Chang of sequences | Exon |
|---|---|---|
| 1 | GGT to AGT | 152 |
| 3 | ATC to TCC | 203 |
| 5 | CGC to CAC | 160 |
| 6 | GGT to AGT | 152 |
| 7 | ATC to TCC | 203 |
| 8 | CGC to CAC | 160 |

## Discussion

Hepatic amoebiasis with the presence of liver abscesses often occur in very large number of patients who may die because the amoeba parasite attacks, multiplies and kills hepatic cells[11]. There are several complications arise with the injury of the outside of the intestines, including an increase in white blood cells, particularly in neutrophils [12].

Our study showed that there was an increase in CRP, GPT, GOT ALP, GGT and bilirubin levels in liver abscesses caused by *E. histolytca*. These findings agreed with (Vineet Jain *et al,* 2017) who found the correlation of various LFT parameters with abscess volume. LFT parameters studied are alkaline phosphatase (ALP), serum albumin, INR, total serum bilirubin and liver enzymes (SGOT, SGPT). These parameters can be related to the disease severity and possible complications [13].

This approach renders the opportunity for early detection of high risk patients and to start early treatment and thus reducing morbidity. Liver infection because of *E. histolytica* may lead to radical changes in the genetic sequence and the change of genetic mutations which probably result in malignant tumors, and these results matched with (Stacey L. Burgess and William A. Petri, Jr. 2016) who reported that the virulence infection with *E. histolytica* to hepatic cells leads to risky influence that may lead to mortality with carcinoma [14]. In the sequence of TP53 gene, the nucleotides changes showed mutations in TP53 gene Exon 147, 152, 160, 203, and 235 amplified from liver cancer samples. The mutation occurred on nucleotides TCC, GGT, ACT, CGC and ATC of TP53 gene; these changes on several exons were found in 6 out of 8 samples of liver abscesses specimens which developed into hepatic carcinoma. These findings were in a harmony with (Krstic, J. et al., 2018) who reported that the importance of p53 in controlling tumorigenesis becomes evident in patients who inherit mutant alleles, a condition known as Li-Fraumeni syndrome, which lead to an extraordinary high, early-onset cancer risks [15].

These changes and genetic mutations were caused by the wrong gene representation caused by *E. histolytica* infections as well as the occurrence of necrotic liver cells. This result was consistent with (Ghosh, S. Padalia, J. And Moonah, Sh.2019) who concluded that *Entamoeba histolytica* is a protozoan parasite that causes amebiasis, which remains a significant cause of mortality and morbidity in the world.

*E. histolytica* causes tissue damage which leads to clinical disease. This review outlines some of the recent advances that have enriched our understanding on the processes that lead to tissue damage caused by *E. histolytica* [16].

 

Liver necrosis and liver cancer cause tissue changes by virulence factor of *E. Histolytica* decomposition factor and occurrence of apoptosis of liver cells as well as changes in liver tissue cells leading to cancer. This finding agrees with (Cornick, S. & Chadee, K. 2017) who concluded that the enzymes produced by these parasites lead to hepatocellular necrosis and cellular apoptosis, as well as genetic mutations that may result in hepatic tissue cell alterations with the incidence of cancers [17].

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