Original article

Evaluation of Serum Alanine Aminotransferase Level in Areca Nut Chewers

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Abstract

Background:
Areca nut chewing is a common social tradition in many regions of the world particularly in Southeast Asia. It is one of the addictive substances that have toxic manifestations in immune, hepatic and other defense systems.

Objective:
To assess the effects of areca nut on liver function by serum alanine aminotransferase (ALT) level in areca nut chewers.

Methods:
This cross-sectional analytical study was conducted in department of Physiology, Rangpur Medical College, Rangpur from July 2022 to June 2023. Total number of 200, age range from 30 to 45 years, were selected after satisfactory inclusion and exclusion criteria. They were divided into two groups. Group A- 100 areca nut chewers, Group B-100 non areca nut chewers. Their liver function status was studied by measuring serum alanine aminotransferase level. For statistical analysis data were analyzed by students t-test, level of significance $p<0.05$, was performed by computer-based software SPSS-25.0 version for windows. A p-value <0.05 was accepted as level of significance. Ethical consideration was achieved by taking an informed written consent after briefing about objectives of the study. Quality was assured through avoidance of missed data, filling of code, regular entry of data and careful data analysis.

Results:
Mean serum ALT level was significantly ($p<0.001$) higher in areca nut chewers than non areca nut chewers.

Conclusion:
The increased serum ALT level in areca nut chewers is evidence of development of hepatic disorders due to areca nut consumption.

Key words: Serum ALT, Areca nut chewers

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Introduction:

Areca nut chewing is a habit of great antiquity. The word "Areca" is derived from the Malay word adakka (areca nut) or from adakeya, the Indian equivalent.[1] Areca nut is the fourth most used social drug, ranking after nicotine, ethanol and caffeine.[2-4]

Areca nut (AN) chewing is common in 10% to 20% of the world population.[5,6] It is estimated that about 600 million people chew various types of areca nut worldwide, predominantly in the countries of South and Southeast Asia.[4,5] Its consumption causes many harmful effects on the human body due to presence of alkaloids in it.[7] These effects of the alkaloids of AN are not only limited to the oral cavity where it comes in to direct contact but may also affect various organs in response to its breakdown and excretion products. Liver is the one among them susceptible to AN induced damage.[8] The areca nut palm (areca catechu) is cultivated mainly in India, Malaysia, Polynesia, Micronesia and most places in the South Pacific Islands. The current production of areca nut in the world is about 0.613 million tons from an area of 0.476 million hectares. India ranks first in area 58% and production 53% of areca nut.[3] Areca catechu has been found to contain mineral, fiber, 50%-60% sugars, 15% lipids

(glyceride of lauric, myristic and oleic acid), 15% condensed tannins (phlobatannin and catechin), polyphenolics
(flavonoids and tannin), and 0.2% - 0.3% alkaloids.[2] Areca catechu contains four areca alkaloids primarily arecoline, along with arecaidine gavacine and guvacoline.[3,8-10] Arecoline (methyl 1-methyl-3,6-dihydro-2H- pyridine-5-carboxylate} acts as an agonist primarily at muscarinic acetylcoline receptors and stimulate the central and autonomic nervous system. This leads to subjective effects of increased well-being alertness and stamina. It is known to improve concentration and relaxation with other reported effects including lifting of mood and cariostatic property.[3,4] It also exerts a direct antimicrobial effect against bacteria, including streptococcus mutans, streptococcus salivarius and various other microorganisms in the oral cavity Arecaidine may have anxiolytic properties through inhibition of gamma amino butyric acid (GABA) reuptake.[3,9,10] Despite these general effects, the adverse effects have outweighed them. Several studies have shown that areca nut chewing is associated with increased risk for various medical conditions including liver cirrhosis, hepatocellular carcinoma, hyperlipidemia, coronary artery disease, hypertension, type 2 diabetes mellitus (DM), oral cancers.[3,8,11,12].

Arecoline, the main areca alkaloid of the areca nut is reported to have cytotoxic, genotoxic and mutagenic effects in various cells.[2-4] Areca nut (arecoline) with or without added tobacco was classified as a group one carcinogen by WHO and International Agency for Research on Cancer (IARC). There is evidence that areca nut without added tobacco causes hepatocellular carcinoma (HCC).[3-5].

The liver is an organ of paramount importance, as it plays an essential role in maintaining the biological equilibrium.[5] The spectrum of liver function includes metabolism of lipid, carbohydrate, protein, vitamins and regulation of blood coagulation. Estimation of enzymes, specific to the hepatic system, gives an assessment of its cellular integrity and functionality by liver function tests.[13] Areca alkaloids produce nitrosamine derivatives which have potential carcinogenic effects.[5] It is stated that the substance present in areca nut increase release of inflammatory mediators including reactive oxygen species, C-reactive protein and tumor necrosis factor-alpha (TNF- alpha), which are risk factors for hepatocellular carcinoma.[14] Studies from the United States of America (USA) and the United Kingdom (U.K), where the South Asian community is large and rapidly growing have shown that areca nut are readily available and commonly used in ethnic enclaves.[2,4] In the USA, this product is legal and inexpensive, thus 20% to 60% of Asian Americans use areca nut. It's use is very uncommon among the other racial groups.[14] The independent and interactive roles of habitual areca nut chewing and other known risk factors for biochemical dysfunction and cirrhosis of the liver are illustrated in this study. Therefore, it was conducted to examine the liver function tests among areca nut chewers. This study served as a good tool in encouraging people not only to quit smoking and alcohol drinking but to also quit areca nut chewing, to reduce their chances of developing cirrhosis. There is a need for further studies to re-investigate this association.

Methods:

This comparative study was performed in Department of Physiology, Rangpur Medical College from July 2022 to June 2023. A total of 200 people were selected through convenient sampling from age 30 to 45 years. The research only included 100 areca nut chewers and 100 non areca nut chewers. The study's subjects provided signed informed consent. Following the random number table approach, two groups were created. Group A – 100 areca nut chewers. And Group B – 100 non areca nut chewers. The patients were assessed using a questionnaire, a clinical examination and biochemical analysis. The standard datasheet suggested for the current research contains all the information, including patient details, clinical assessment and biochemical investigations. To provide a comparison study between areca nut chewers and non areca nut chewers, results were compared and summarized. Students t-test applied to compare the significant differences regarding efficacy of both groups using SPSS 25 version. Level of significance is $p<0.05$.

Results:

Table-I showed no significant age difference between two groups. Mean±SD of age were 36.37±1.535 and 36.74±1.580 years in group A and B respectively.

Table-I: Showing mean±SD of age, height, weight and body mass index of the study subjects in different groups

Age in years	Group A (n=100)	Group B (n=100)	p-value
Mean±SD	36.37±1.535	36.74±1.580	>0.005
Range	30-42	30–40	

Mean±SD of serum alanine aminotransferase level is 54.73±9.887 and 30.74±5.368 U/L in group A and B respectively. In this study, the mean serum ALT level was significantly higher (p<0.001) in areca nut chewers than those of non areca nut chewers (Table-II).

Table-II: Serum alanine aminotransferase level (ALT) of the study subjects in different groups

Serum ALT	Group A (n=100)	Group B (n=100)	p-value
Mean±SD (U/L)	54.73±9.887	30.74±5.368	<0.001
Range	38-88	22-38	

Discussion:

In this study, the mean serum alanine aminotransferase (ALT) level were significantly higher (p <0.001) in areca nut chewers than those of non areca nut chewers. These findings are in aggrement with those reported by Singroha K and Kamath VV,[8] Garg A, Chaturvedi P and Gupta PC,[11] Khashage SD, Juneja S. and Bhowate RR,[15] Shafique K et al.[16] Ramya M and Anuradha R[17] and Wu F, Parvez F and Chen Y[18] Singroha K and Kamath VV[8] reported increased level of serum alanine aminotransferase in areca nut chewers might be due to increased oxidative stress and increased lipid peroxidation lead to damage of liver tissue.

Gupta PC et al[11] reported that areca nut contains hepatotoxic substances including arecoline, reactive oxygen species (ROS) such as super oxidea anions, hydroxyl radicles hydrogen per oxide and HOCL can damage cellular constituents leading to inflammation and injury of the liver may lead to increased serum alanine aminotransferase level in areca nut chewers. Khashage SD, Juneja S. and Bhowate RR[15] found several risk factors in areca nut chewers which are responsible for development of liver diseases leads to increase level of serum alanine aminotransferase. Shafique K et al[16] reported that areca nut also increases the production of pro inflammatory cytokines (IL- 1,IL-6 and TNF- a). that would be involved in liver cell injury. This causes impairment of liver functions and increased serum ALT level. Ramya M and Anuradha R[17] foumd that arecoline propagates the lipid peroxidation which damage the biological cell membrane of liver and enzymes are leaked out in to blood and increases the level of serum alanine aminotransferase. Wu F, Parvez F and Chen Y[18] suggested that serum alanine aminotransferase level is higher in areca nut chewer might be due to the chemical present in areca nut cause oxidative stress on the liver which leads to damage liver cells. In the present study, increased level of serum alanine aminotransferase in areca nut chewers may be due to increased oxidative stress and lipid peroxidation leads to damage liver tissue. Areca nut also increases production of pro inflammatory cytokines (IL-1, IL-6, TNF-a) that may be involved in liver cell injury. Areca nut also contains hepatotoxic substances including arecoline, reactive oxygen species (ROS) such as super oxide anions, hydroxyl radicles hydrogen per oxide and HOCL can damage cellular constituents leading to inflammation and injury of the liver may lead to increased serum alanine aminotransferase level in areca nut chewers. For these causes, there is increased level of serum alanine aminotransferase level in areca nut chewers than non areca nut chewers.

Conclusion:

The elevated serum ALT levels observed in individuals who chew areca nut serve as an indication of the onset of hepatic disorders associated with areca nut consumption. The effects on additional liver enzymes, serum albumin, and prothrombin time may illustrate both the acute and chronic effects on liver function; however, further research involving a larger sample size is necessary.

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