



SMOKELESS TOBACCO;

SERUM FERRITIN AND VITAMIN B12 IN RELATION TO C REACTIVE PROTEIN IN INDIVIDUALS. HYDERABAD SINDH BASED STUDY.

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Article received on:

12/05/2017

Accepted for publication:

15/07/2017

Received after proof reading:

08/09/2017

ABSTRACT... Objectives: To know the serum ferritin and vitamin B12 levels in relation to C reactive protein in individuals using smokeless tobacco in Hyderabad, sindh, Pakistan. **Study Design:** Cross sectional study. **Place of Study:** Private clinics of consultants of Hyderabad, Sindh, Pakistan. **Duration of Study:** January 2016 to February 2017. **Methodology:** One hundred eighty three individuals were selected from different clinics of physicians, dental surgeons of sadder Hyderabad sindh Pakistan by judgmental sampling. Patients were young subjects, mean age was 21.4 ± 7.4 years, mean BMI was 22.1 ± 3.8 and mean duration of chewing tobacco was 2 ± 1.5 years. All types and forms of gutka, manpuri and flavored betel nut were included like bombart, zafri and panparag. The dose was 30-100grams once or two times. SPSS 16 was used as stational software and Chai square test was used to calculate p value. P value was taken <0.05 statically significant. **Results:** Frequency of use of gutka was 32%, Betel nut 38% and 29% had habit of chewing manpuri. Serum ferritin was low and c reactive protein was high, p value was <0.05 in gutka and manpuri users. Vitamin B12 was reduced significantly in gutka user p value was <0.05 . In betel nut chewers significant finding was only high C reactive protein, p value <0.04 . **Conclusion:** Smokeless tobacco has significant negative impact on serum ferritin and vitamin B12 levels. These chewing agents also increased inflammatory markers like c reactive protein.

Key words: Manpuri, Betel Nut, Gutka, Hyderabad, Sindh.

Article Citation: Shaikh IA, Masood N, Sheikh FA, Shaikh T. Smokeless tobacco; serum ferritin and vitamin B12 in relation to C reactive protein in individuals. Hyderabad Sindh based study. Professional Med J 2017;24(9):1310-1315.
DOI: 10.17957/TPMJ/17.4045

INTRODUCTION

Chewing smokeless tobacco is commonest addiction in Pakistan and Southeast Asia for many years. Betel leaf chewing with areca and tobacco or without tobacco is frequently used in the South Asian region, significantly in China and Taiwan along with New Guinea and Thailand.¹

Betel nut is being used by millions of people in the world.² it is the even the commonest addictive product introduced all over the world.³

A survey from various countries including Pakistan demonstrated the prevalence of betel nut items in past decades ranged between 20 to 40% in adults.⁴

A study conducted at Karachi by Khawaja and others mentioned forty percent people having

regular habit of using betel nuts.⁵

Mainpuri, contains betel nut, camphor, tobacco, cinnamon, clove, slaked lime as its major ingredients.⁶

Unfortunately all ages and class of society even students are addicted to Mainpuri in different forms.

The local Mainpuri contains a high percentage of known hydrocarbon generating substances which have a carcinogenic effect.⁷

Gutka is made up of mashed areca nut, some flavored substance, liquid lime and impure sweet and some crushed leaf of PAAN.⁸ it is virtually a poison. It has been promoted as a mouth freshener but this mixture is a combination of 4,000

chemicals of which at least 40 are carcinogenic compounds.⁹

In Pakistan, 8.5 to 10 times increased risk of oral cancers because of chewing tobacco, eating pan, gutka, betel nut.¹⁰

Surprisingly 7% of primary school children eat gutka and 96% women living on coastal area of Karachi consume gutka while they breastfeed their child.¹¹

Anemia is defined when hemoglobin reduced less than 13 g/dl in male and less than 12g/dl in females.¹²

In a survey of our country showed, 50.4 % of non-pregnant women have iron deficiency anemia. According to demographic statics 49.3% in Urban and 50.9% in rural women are suffering from anemia.¹³

Smokeless tobacco is a causative agent in obstructive lung diseases for example it aggravates the asthma also. It may impair the status diabetes mellitus due to reduced adiponectin levels.

Some studies linked smokeless tobacco use in increased incidence of still birth and low birth weight.¹³

Obviously multiple oral mucosal disorders which may extend beyond the oral cavity in gutka users.¹⁴

Deficiency of iron and vitamin B complex other trace elements due to nutritional depletion could possibly initiate anemia and altered cell-mediated immunity, which in turn acts as a promoting factor to this preexisting pathologic response of the lamina propria¹⁵ in chewing smokeless tobacco.

The inflammatory cells in gutka user showed increased percentage of neutrophils and decreased percentage of lymphocytes and inflammatory effects smokeless tobacco on lungs is well documented.¹⁶

The rationale of this study is to know the levels

of serum vitamin B12, serum ferritin, C reactive protein in mapuri, gutka and betel nut user because these substances produce varying degree of anaemia and inflammatory response.

METHODOLOGY

The cross-section observational study was conducted at different clinics of sadder Hyderabad sindh from January 2016 to February 2017

The sample size was based on judgmental sampling, 183 patients were selected, 102 were female (56%) and 81 were male (44%) from different clinics of sadder Hyderabad which was a biggest area of consultants of province and cover all patient seeking advice from whole province, sindh.

Inclusion criteria

Young individuals 18-40 years.

Taking betel nut, gutka or manpuri at least 18 months.

Exclusion criteria

Raised CRP due to other causes.

Diagnosed case of anemia or taking any hemopoietic substance like iron or vitamin B12.

Co morbidities like cardiac, renal or inflammatory bowel diseases.

Patients already had oral cancers or sub mucosal fibrosis.

Patients were young subjects, mean age was 21.4 ± 7.4 years and mean duration of chewing tobacco was 2 ± 1.5 years. All types and all forms of gutka, manpuri and betel nut were included like bombart, zafri and panparag. The dose was 30-100grams once or two times. Mean BMI was 22.1 ± 3.8 .

Serum ferritin was considered low if was less than 15mg/dl in male or less than 7mg/dl in female while serum B12 was considered low if less than 170ug/dl. C reactive proteins was considered high, if more than 6mg/dl.

Patients base line characteristics were noted along with serum ferritin, vitamin B12 and C reactive proteins.

Data was plotted SPSS 16.0, chi square was used to calculate p value in male and female biochemistry in different groups. P value was considered <0.05 significant.

RESULTS

Out of one hundred eighty three, 56% were female and 44 % were males were belonging to different areas of Hyderabad. Among them, 52% was married and belonged to low income areas like penjra pole and liaquat colony. The male to female ratio was 1:1.2.

Frequency of use of gutka was 32%. Betel nut 38%, 29% had habit of chewing manpuri, respectively.

Serum ferritin was low p value was <0.05 and c

reactive protein was high <0.05 in gutka chewer Table-II.

While no significant difference seen in betel nut chewer in serum ferritin and B12 level but C reactive protein was high than normal p value <0.04 Table-III.

In manpuri chewer two parameters were significantly disturbed serum ferritin, p value was <0.05 and high c reactive protein was also significant <0.05. Table-IV.

Reduced level of vitamin B12 in manpuri user although p value was not significant p >0.06 but B12 was reduced significantly in gutka user p value was <0.05.

| Variables | Gutaka | Mainpuri | Flavored Betel nut | Percentage |
|-------------------------------------|--|------------------------------------|-------------------------------------|------------|
| Male | 32 | 25 | 24 | 44 |
| Female | 27 | 28 | 47 | 56 |
| Age | 22±3.7 | 25±8.5 | 28±12.3 | |
| Married | 20 | 35 | 40 | 52 |
| BMI | 22.±1.5 | 21±2.4 | 24±2.7 | |
| Town /city | Liaquat colony/penjra pool/hussainabad | Qasimabad/latifabad/Liaquat colony | Latifabad 6,7,8,9 Defence /garrison | |
| Duration of tobacco chewing (years) | 2±1.5 | 3±2.1 | 10±4.5 | |
| Serum ferritin | 12.1±2 | 10±4 | 18±4.5 | |
| Serum B12 | 177±10 | 190±11.3 | 180±14.5 | |
| CRP<6mgdl | 5±1.3 | 4±2.5 | 5±1.2 | |

Table-I. Base line characteristics of 183 patients from Hyderabad

| Variables | Male | Female | P value |
|--------------------|-----------|----------|---------|
| number | 32 | 27 | |
| Serum ferritin | 12.5±20.1 | 7.8±10.5 | <0.05 |
| Vitamin B12 | 190±6.4 | 170±10.5 | <0.05 |
| C.reactive protein | 4.5±± | 5.1± | <0.05 |

Table-II. Biochemical profile of Gutka users N =59 (32%)

| Variables | Male | Female | P value |
|--------------------|----------|----------|---------|
| Number | 25 | 28 | |
| Serum ferritin | 12±15.3 | 10±10.3 | <0.05 |
| Vitamin B12 | 210±10.2 | 150±11.2 | <0.06 |
| C.reactive protein | 6±1.3 | 5.5±2.5 | <0.05 |

Table-IV. Biochemical profile of Manpuri users (N= 53(29%))

| Variables | Male | Female | P value |
|--------------------|--------|----------|---------|
| Number | 24 | 47 | |
| Serum ferritin | 30±11 | 15±10.3 | >0.06 |
| Vitamin B12 | 210±20 | 190±19.3 | >0.07 |
| C.reactive protein | 5±2.9 | 4.5±8.0 | <0.04 |

Table-III. Biochemical profile of betel Nut (Chalia) users (N=71(38%))

DISCUSSION

Evidences are accumulating that areca (betel nut) products produce dependency and included in "substance induced disorders" in DSM IV.¹⁷

Unfortunately South Asia is facing storm of using smokeless tobacco recently.¹⁸

In Pakistan, prevalence of chewing tobacco in

young adults shown 16.1% to 20%.¹⁹

Age group for these cases varies from region to region. It is very common in teen age group. A study of Saipan showed, 8.8% teenagers with mean age as 16.3 years \pm 1.5 were being involved in smokeless tobacco use.²⁰

In our study, patients were young subjects and mean age was 21.4 \pm 7.4 years.

In addition, a female dominancy is evident for use of areca nut was reported in this region. Some studies in our country showed a male female ratio of 1:2.5 or 3:4²¹

In our study 102 were female (56%) and 81 were male (44%), ratio was 1.2:1 which is slightly low than above mentioned study.

In our study the novel observation was high C reactive protein, <0.05 in gutaka chewer while in betel nut chewer C reactive protein was high than normal p value <0.04. In mainpuri high c reactive protein was also significant <0.05. It indicates the increased inflammatory markers in smokeless tobacco user and it also observed internationally.

A recent study carried out in India showed that chewing even a slight amount of tobacco could cause narrowing of major heart arteries by over 14%.²²

The findings also reflect an increased risk of developing coronary artery disease/ or other cardiovascular complications in smokers and gutka users.²³

In one study increased mean level of homocysteine in the group which consumed Smokeless tobacco along with betel nut. In this group it appeared to be due to decreased concentrations of folate and vitamin B12.²⁴ This study supports the findings of our study which shown reduced level of vitamin B12 in manpuri user although p value was not significant p >0.06 but B12 was reduced significantly in gutaka user where the p value was <0.05.

In Bangladesh, people start gulping the juice of the tobacco. This leads to haemoglobin levels as low as 6-7%.²⁵ In our study the anemia was evident, serum ferritin was low in gutka and mainpuri user, p value was <0.05.

Few studies are against the decreased hemoglobin and vitamin B12 in gutaka user like Study by Jaganmohan et al that showed increased haematological parameters in smokeless tobacco drivers²⁶ but another study supported our findings that there is negative effect of gutkha on blood hematology.²⁷

Iron deficiency anemia is commonly seen in patients using betel nut because of its ingredient, Arecoline.²⁸

CONCLUSION

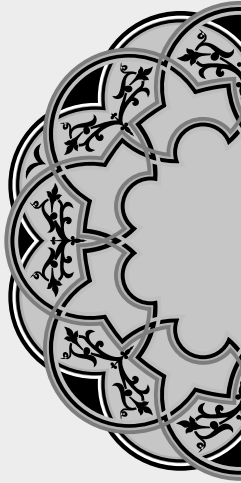
Smokeless tobacco has significant negative impact on serum ferritin and vitamin B12 levels. These chewing tobacco substances also increase inflammatory markers like c reactive protein.

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REFERENCES

1. Tilakaratne WM, Klinikowski MF, Saku T, Peters TJ et al. **Oral submucous fibrosis: review on aetiology and pathogenesis.** Oral Oncol. 2006;42(6):561-8.
2. Pankaj C. **Areca nut or betel nut control is mandatory if India wants to reduce the burden of cancer especially cancer of oral cavity.** Int J Head Neck Surg. 2010;1:17-20.
3. Gupta PC, Ray CS. **Epidemiology of betel quid usage.** Ann Acad Med Singapore. 2004;33(4) :S31-6.
4. Mahmood Z. **Chewing and smoking habits of the people of Karachi - 1981.** J Pak Med Assoc. 1982;32:34-7.
5. Khawaja MR, Mazahir S, Majeed A, Malik F, Merchant KA, et al. **Knowledge, attitude and practices of a Karachi slum population regarding the role of products of betel, areca and smokeless tobacco in the etiology of head and neck cancers.** J Pak Med Assoc. 2005;55:S41.
6. Punnya V. Angadi, K. P, Rekha. **Oral submucous fibrosis: a clinicopathologic review of 205 cases in Indians.** Oral and Maxillofacial Surgery. 2011;15(1):15-19.

7. ANI First Published: Saturday, January 28, 2012 - 15:32
8. **CPAA: Quit Smoking Campaign, Anti Tobacco & Quit Smoking Campaign**". Retrieved 30 May 2015.
9. **CDC, Fact Sheet - Betel Quid with Tobacco (Gutka) - Smoking & Tobacco Use**". Smoking and Tobacco Use. Retrieved 30 May 2015.
10. Baig S, Lucky MH, Qamar A, Ahmad F, Khan S, Ahmed W, et al. **Human Papilloma Virus and Oral Lesions in Gutka Eating Subjects in Karachi**. JCPSP 2012;(3): 135-8.
11. Kamal R. **Gutka: Taste for the toxic**. The Express Tribune, 3rd march ; 2012.
12. McLean E, Cogswell M, Egli I, Wojdyla D, De Benoist B. **Worldwide prevalence of anaemia, WHO vitamin and mineral nutrition information system, 1993–2005**. Public health nutrition. 2009;12(04):444-54.
13. National Nutrition Survey 2011, Planning Commission, Planning and Development Division, Government of Pakistan.
12. WHO/UNICEF/UNU. **Iron deficiency anemia, assessment, prevention and control: a guide for programme managers**. WHO; 2001.
13. Imam SA, Nawaz H, Sepah YJ, Pabany AH, Ilyas M, Ghaffar S. **Use of smokeless tobacco among groups of Pakistani medical students – a cross sectional study**. BMC Public Health 2007;7:231.
14. Javed F, Chotai M, Mehmood A, Almas K. **Oral mucosal disorders associated with habitual gutka usage: a review**. Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology and Endodontics 2010;109(6):857–864.
15. M. Ahmad, S. Ali, A. Ali, and K. Chaubey, "Epidemiological and etiological study of oral submucous fibrosis among gutkha chewers of Patna, Bihar, India," Journal of Indian Society of Pedodontics and Preventive Dentistry, vol. 24, no. 2, pp. 84–89, 2006.
16. Jensen EJ, Pedersen B, Frederiksen R, Dahl R. **Prospective study on the effect of smoking and nicotine substitution on leukocyte blood counts and relation between blood leukocytes and lung function**, Thorax, 1998; 53: 784-789.
17. Substance related disorders. In Charles W Mitchell, editor. **Kaplan and Sadock's Synopsis of Psychiatry: behavioral sciences/Clinical psychiatry**. 8th ed. Maryland: Lippincott Williams and Wilkins 1998; pp 375-91.
18. Gupta PC, Ray CS (2003) **Smokeless tobacco and health in India and South Asia**. Respirology 8(4): 419–31.
19. **Smokeless tobacco major source of oral cancer**. DAWN. 2011-05-31.
20. Oakley E, Demaine L, Warnakulasuriya S. **Areca (betel) nut chewing habit among high-school children in the Commonwealth of the Northern Mariana Islands (Micronesia)**. Bull World Health Organ. 2005;83(9):656-60.
21. Aziz SR. **Oral submucous fibrosis: an unusual disease**. J N J Dent Assoc. Spring 1997; 68 (2): 17-9. 5
22. Mohammad Perwaiz Iqbal, Mohsin Yakub. **Smokeless Tobacco Use: A Risk Factor for Hyperhomocysteinemia in a Pakistani Population**. PLOS one; 2013; 12
23. Ramakrishnan S, Thangjam R, Roy A, Singh S, Ramakrishnan L, et al. (2011) **Acute effects of tobacco chewing on the systemic, pulmonary and coronary circulation**. Am J Cardiovasc Drugs 11(2): 109–14
24. Critchley JA, Unal B. **Is smokeless tobacco a risk factor for coronary heart disease? A systematic review of epidemiological studies**. Eur. J. Cardiovasc. Prev. Rehabil. 2004 Apr; 11(2):101-12.
25. **Tobacco behind alarming rise in cancer cases among women**. World no Tobacco Day. The Times of India Ahmed Abad; May 2010; 4.
26. P. Jaganmohan* and A. Phaninanatha Sarma, **Studies on changes in hematological and biochemical parameters in smokeless tobacco (Gutka) chewing auto drivers in Nellore district of Andhra Pradesh, India**. Journal of Applied and Natural Science, 2011, 3 (1): 106-107.
27. Roan Mukherjee¹ and Amal Chatterjee. **Assessment of the effects of smoking and consuming gutka (smokeless tobacco) on selected hematological and biochemical parameters: a study on healthy adult males of hazaribag, jharkhand**. IJPCBS 2013, 3(4), 1172-78.
28. Strickland SS, Veena GV, Houghton PJ, Stanford SC, Kurpad AV. **Areca nut, energy metabolism and hunger in Asian men**. Ann Hum Biol. 2003; 30(1):26–52.



*“Sometimes the wrong choices
bring us to the right places.”*

Unknown

AUTHORSHIP AND CONTRIBUTION DECLARATION

| Sr. # | Author-s Full Name | Contribution to the paper | Author=s Signature |
|--------------|---------------------------|----------------------------------|---------------------------|
| 1 | Imran Ali Shaikh | Hypthesis, Critical analysis | |
| 2 | Naila Masood | Final version of manuscript | |
| 3 | Fouzia Aijaz Sheikh | Writing manuscript | |
| 4 | Talha Shaikh | Collection of cases | |