

## Betel Nut Consumption Leading To Poor Control of Post Prandial Blood Glucose Levels In Diabetics: Indication of A Probable Role of Gaba Receptors In Regulation Of Blood Glucose Levels



### Biochemistry

**KEYWORDS :** Cubitus varus deformity, lateral closing wedge osteotomy, k wire fixation

**Dr Addanki Yohoshuva**

MD, Professor of Biochemistry

**Dr M A Bari Siddiqui**

Assistant Professor of Biochemistry

### ABSTRACT

*Diabetes is a major health concern worldwide, social habits are an important part of its etiology and poor glycemic control is a major contributor of associated morbidity. Betel nut (Areca catechu) is chewed regularly by at least 10% of the world population. The alkaloids or nitrosated compounds present inside act as competitive inhibitors of GABA receptors and have widespread effects in the body, including actions on the brain, cardiovascular system, lungs, gut and pancreas. Increased central obesity is also found in association with betel usage in man. The effects of chronic betel usage in man are at least as diverse as those of smoking and the habit increases the risks of ill health. In view of the above theory the present study was conducted in department of biochemistry Siddhartha Medical College, Vijayawada and Bhaskar Medical College, Yenkepally. A total of 70 patients were enrolled in the study with an aim to document the usage and effects of betel nut chewing in diabetic patients. The majority of patients with diabetes were in the older age group (>45 years) and many of them were overweight or obese. Those who were habituated to betel nut chewing showed poor glycemic control as evidenced by the high mean of post prandial blood sugar of 160mg/dl ( $p < 0.001$ ) and HBA1C levels of  $> 7\%$  ( $p < 0.001$ ) where as the fasting blood sugar levels had no significant differences ( $p > 0.001$ ). As most of the times betel nut is taken after food and on the balance of evidence we can say that chronic consumption of betel nut in diabetic people is a contributing factor for poor control of post prandial blood sugar levels. The possible mechanism is by inhibition of GABA receptors on pancreas. There is necessity of further work in the probable mechanism of poor control.*

### Introduction

Diabetes is a major health concern worldwide and social habits are an important part of its etiology. Since Paan (beetle leaf) consumption is a psychoactive and addictive habit and is used by about 600 million people worldwide<sup>1</sup>. Production wise, India tops the list of major betel nut producing countries followed by China and Myanmar. India also leads the major betel nut consuming countries' list with almost the entire list comprising of the countries from Asian continent<sup>2</sup>. Several mechanisms have been identified by which the specific alkaloids of the *Areca catechu* nuts, chewed alone or within Paan 'quids' or 'chews' made by wrapping chopped betel-nut, sea shells or slaked lime, and sometimes other ingredients, in a leaf of the piper beetle vine produce physical and psychological effects<sup>3</sup>. Users report increased well-being and a soothing effect on the digestion, protection of the mouth and gums and some euphoria and hence used on many social occasions after food<sup>4</sup>. Acute ill effects are also reported at high rates of usage and include cardiac arrhythmia, exacerbation of asthma, acute psychosis and acute gut upset<sup>5</sup>. There are four main arecal alkaloids, arecoline, arecaidine, guvacine and guvacoline. Arecal alkaloids have anti-muscarinic effects on smooth muscle, especially arecoline. They also bind to GABA receptors in the brain, contributing to their psychoactive effects<sup>6</sup>. GABA receptors are chloride channels, similar in structure to acetylcholine receptors and are found in many tissues of the body, including pancreatic islets, where areca alkaloids can also be expected to have physiological effects; for example, arecaidine is as active as GABA in stimulating collagen synthesis by buccal fibroblasts<sup>7</sup>. Arecoline is not a simple activating ligand for the GABA receptor since it acts as a GABA receptor 'blocker', preventing normal GABA inhibition of neurotransmission<sup>8</sup>. There is a report of severe extra pyramidal symptoms in association with phases of unusually heavy betel quid usage thought to be due to antagonism of the anti cholinergic agent procyclidine by arecoline<sup>9</sup>. The immediate effects of betel quid chewing include palpitations, sweating and facial flushing with a feeling of skin warmth. Objective studies have confirmed that facial skin temperatures rapidly increase by 0.5 to 2°C with betel use<sup>10</sup>. While the pulse rate increases, whether or not the user is habituated to betel use, increases in blood pressure are only seen in novices<sup>11</sup>. Areca nut has also been reported to induce higher basal secretion of catecholamines from adrenal chromaffin cells than other paan

ingredients<sup>12</sup>.

Chewing juices can, *in vitro*, inhibit the secretion of catecholamines in response to carbachol or high potassium concentrations, suggesting paan components may affect the entry of Ca<sup>2+</sup> into cells through high-voltage channels<sup>13</sup>. One of the GABA shunt enzymes, glutamate decarboxylase (GAD) is also found in islet cells and is an antigen strongly associated with the appearance of GAD antibodies at the onset of type I diabetes in man<sup>14</sup>. Since arecal alkaloids act as GABA receptor inhibitors they could, by blocking the inhibitory effects of GABA on glucagon and somatotrophin secretion, increase their release. An immediate effect is of a rise in glucagon with hyperglucagonaemia. This is a mechanism, therefore, that might be capable of leading to hyperglycaemia, or eventual diabetes, over time. Reduced expression of GAD is produced by GABA inhibition and this in turn reduces autoimmune responses to GAD in rat islets and brain<sup>15</sup>. One feature common to diabetogenic nitrosocompounds, including STZ, is that they each contain a moiety with a 'ring' structure similar in configuration to the chair-shaped 'ring' of hexameric glucose. It is this part of the molecule that may, by binding to islet beta cell glucose receptors, account for their diabetogenicity<sup>16</sup>. Similar findings are reported for dietary sources of nitroso-compounds. Increased maternal intake of nitrosamines being associated with increases in childhood type I diabetes in man<sup>17</sup>.

The effect of areca feeding on glucose tolerance and on the pancreatic islets has been investigated in the mouse<sup>18</sup>. 8.3% of betel-fed adults developed permanent hyperglycaemia, central obesity and islet enlargement with beta-cell changes typical of human type II diabetes in contrast to an incidence of diabetes of 0.5% in the colony as a whole and in control-fed animals. Areca consumption could increase the risk of the development of diabetes in man was established by a study showing hyperglycemia in relation to paan usage and other recognized risk factors for type II diabetes in adult Bangladeshis living in Tower Hamlets, east London, between 1991 and 1993<sup>19</sup>. Thus there is a theoretical basis for suspecting that areca nut might well prove to be a diabetogenic item of diet. In view of the above theory the present study was conducted in department of biochemistry Siddhartha Medical College, Vijayawada and Bhaskar Medical College, Yen-

kepally. A total of 70 patients were enrolled in the study. The aim of the study was to document the usage and effects of betel nut chewing in diabetic patients attending the hospital.

**Materials and methods**

This study was conducted in department of Biochemistry, Sidhartha Medical College, Vijayawada and Bhaskar Medical College, Yenkepally from June 2013 to May 2015. A total of 70 patients who had documented Diabetes Type II and were on treatment were enrolled after taking their consent. All the enrolled patients were interviewed and their medical history was taken. It was estimated that 50% of diabetic patients are betel nut chewers with a 95% confidence interval of 44% to 56%. Patients on treatment with Insulin or having other co-morbid conditions were excluded from the study. Those enrolled were divided into two groups, Betel nut chewers and Non chewers. Blood investigations were done at the time of diagnosis and after three months of follow up in both the groups. Blood samples were taken in Oxalate-NaF for blood glucose estimation and in plain tubes or HbA1C. Both fasting and post prandial blood glucose within 2 hours after food and was estimated along with HbA1c<sup>20</sup>. Blood glucose was estimated using GOD POD method<sup>21</sup> and HbA1C using Ion Exchange Resin Method.

**Results**

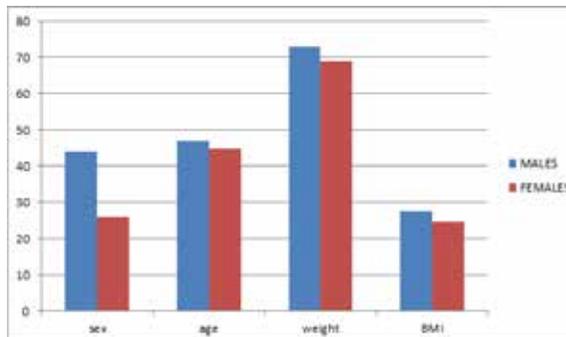
**Age, sex, weight and BMI**

Of the 70 diabetic patients, there were 44 males and 26 females with their ages ranging from 25 to 78 years (at the time of their diagnosis). The majority (60%) of the patients were aged 45 years and above. The mean age, median age and interquartile range were respectively 47, 49 and 40 - 55 years for males and 44.9, 45.0 and 38-54 years for females. In each age group, there were more male than female patients. Those under 35 years old account for 11% of the cases while 40% of the patients were in the 45-54 years age group and 22% were aged 55 years and above. The maximum and minimum weights recorded at diagnosis were 92 and 38 kg respectively. The overall mean, median and interquartile range for weight was 69, 71 and 63-78 kg respectively at diagnosis. The mean weight and interquartile range for males and females were 73, 64-82 and 69, 60-74 kg respectively (Table 1, figure 1).

The highest and lowest BMI were 40 kg/ m<sup>2</sup> and 17 kg/m<sup>2</sup> with the overall mean and interquartile range 26 kg/m<sup>2</sup> and 23-28 kg/ m<sup>2</sup> respectively. The mean and interquartile range for males were respectively 27.6 kg/ m<sup>2</sup> and 25-30 kg/m<sup>2</sup>, and for females 24.7 kg/m<sup>2</sup> and 23-31 kg/m<sup>2</sup> as shown in table 1 and figure 1. Of the 70 diabetic patients from whom a family history was obtained, 25 (35.7%) had a positive family history of diabetes. 7 of the 25 (28%) had one parent and 12 (48%) had a brother or sister with diabetes, and the others had a parent plus a sibling with diabetes. There were 35% of men and 36% of women with a family history of diabetes mellitus. Overall, 74% of diabetic patients were chewing betel nut before and continued doing so after their diagnosis. Betel nut chewing was more among females who constituted 79% when compared to males who constituted 67%. Amongst the chewers the majority (57%) of patients used less than 5 betel nuts per day and only 23% chewed 5-9 nuts per day and 19% 10 or more nuts per day.

**Table 1: age,sex , weight and BMI**

	Number	Age		Weight		BMI	
		Mean	Inter-quartile range	Mean	Inter-quartile range	Mean	Inter-quartile range
MALES	44	47	40-55	73	64-82	27.6	25-30
FE-MALES	26	45	38-54	69	60-74	24.7	23-31



**Blood glucose level**

Fasting and post prandial levels were estimated at time of diagnosis and most recent i.e 3 months post diagnosis. In betel nut chewers at the time of diagnosis the overall mean fasting blood glucose level was 156.2 mg/dl with an interquartile range of 119-202 mg/dl. The mean fasting glucose was 148.3 mg/dl for males and 166 mg/dl for females. The interquartile range for males was 112 -211.3 mg/dl and for females 108-224.7 mg/dl. The means of the most recent fasting blood glucose level overall were 89.8mg/dl with interquartile range of 117.7- 182.1 mg/dl. The mean and interquartile range in males and females were 87 and 92 mg/dl respectively and the interquartile ranges were 72.2 - 140.4 mg/dl for males and 69 to 154.2 mg/dl in females. In non-chewers at the time of diagnosis the overall mean for fasting glucose was 150.2 with an inter quartile range of 117.5- 198.2 mg/dl. The mean and interquartile ranges of fasting blood glucose for males were 152.4 mg/dl, 110.4 – 216.2 mg/dl and in females were 148.6 mg/dl, 109.1 – 232 mg/dl . After 3 months the overall mean and interquartile ranges of fasting blood glucose were 92.6 mg/dl and 112 – 176.5 mg/dl. The mean and interquartile range in males was 78.1 mg/dl, 68.6 – 139.9 mg/dl and in females were 90.7 mg/dl, 71.6 – 149.9 mg/dl. the difference in fasting levels between betel nut chewers and non chewers after 3 months was statistically not significant with P >0.001. In betel nut chewers at the time of diagnosis the overall mean post prandial blood glucose level was 255.6 mg/dl with an interquartile range of 180-288 mg/dl. The mean post prandial blood glucose levels at the time of diagnosis were 270 mg/dl for males and 244.8 mg/dl for females. The interquartile range for males was 203.4 -298.8 mg/dl and for females 180-293.4 mg/dl. After three months the overall mean and interquartile range was 189.8mg/dl, 141- 248.2 mg/dl respectively. The means of post prandial blood glucose level in males and females were 185 and 191 mg/dl respectively and the interquartile ranges were 142.2-240.4 mg/dl for males and 139 to 254.3 mg/dl in females. (Table 2, figure 2).

In non-chewers at the time of diagnosis the overall mean and interquartile range was 224.4 mg/dl, 168-261.2 mg/dl respectively. In males and females the means were 236mg/dl and 218.1 mg/dl with the respective interquartile ranges of 172.2-262.4 mg/dl for males and 164.4-251.3 mg/dl for females. After three months the levels in post prandial blood sugar were slightly lower than in betel nut chewers with overall mean and interquartile range of 151.7 mg/dl, 114 – 172.9 mg/dl respectively. Mean and interquartile ranges for males were 142.3 mg/dl, 106.4 – 182.1 mg/dl and in females were 158.6 mg/dl, 114 – 172.9 mg/dl. The difference in post prandial blood glucose levels at three months between betel nut chewers and non chewers was statistically significant with p<0.001. (Table 3, figure 2).

**Table 2: blood glucose in betel nut chewers**

Category	Betel nut chewers (all values are in mg/dl)							
	Time At diagnosis				After 3 months			
	Fasting		Post prandial		Fasting		Post prandial	
Sex	Male	Female	Male	Female	Male	Female	Male	Female
Mean	148.3	166	270	244.8	87	92	185	191

Inter-quartile range	112-211.3	108-224.7	203.4-298.8	180-293.4	72.2-140.4	69-154.2	142.2-240.4	139-254.3
----------------------	-----------	-----------	-------------	-----------	------------	----------	-------------	-----------

**Table 3: blood glucose in non chewers**

Category	Non chewers (all values are in mg/dl)							
	At diagnosis				After 3 months			
Time	fasting		Post prandial		fasting		Post prandial	
	Male	Female	Male	Female	Male	Female	Male	Female
Mean	152.4	148.6	236	218	78.1	90.7	142.3	158.6
Inter-quartile range	110.4-216.2	109.1-232	172.2-262.4	164.4-251.3	68.6-139.9	71.6-149.9	106.4-182.1	104.9-176.4

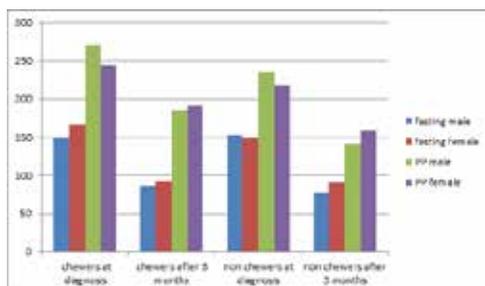


Figure 2: mean of blood glucose levels in diabetic betel nut chewers and non chewers

In betel nut chewers the mean HbA1c after three months was 8.1 with interquartile range 7.1 - 9.8, and a minimum and maximum level of 5.8 and 12.2 respectively. Males had better control with mean HbA1c levels of 7.9 with interquartile range of 5.7 to 9.2 whereas females had mean HbA1c levels of 8.3 and interquartile ranges of 6.3 - 11.0. In non chewers the mean and interquartile ranges were 7.6, 5.6 - 8.8 with no significant difference between male and female with their respective means and interquartile range being 7.2 and 7.4, 5.3-8.3 and 5.2 - 8.5, P>0.001. The difference in HbA1c levels in betel nut chewers and non chewers was statistically significant with P <0.001. Only 17% of men and 23% of women in the study had fairly good control of their blood glucose (<180mg/dl). 80% of patients had poor control of their blood glucose level (>180 mg/dl). Of the 56 diabetic patients with poor control of their blood glucose level, 41 (73.2%) were betel nut chewers. (Table 4, figure 3).

**Table 4: HbA1c levels**

	Betel nut chewers		Non chewers	
	Male	Female	Male	Female
Mean	7.9	8.3	7.2	7.4
Interquartile range	5.7-9.2	6.3-11	5.3-8.3	5.2-8.5

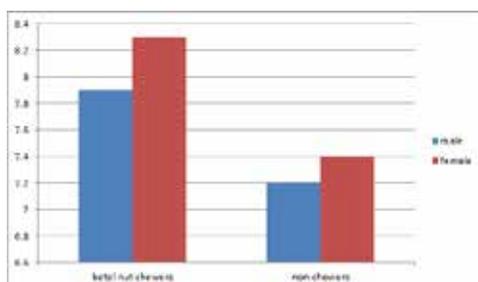


Figure 3: HbA1c comparison

**Discussion**

Most of the patients came from either Hyderabad or Vijayawada city and had adapted an urban lifestyle. We have observed that Diabetes mellitus is more common in the older age group and in those who have lived in urban centers for a long time and have adopted a more western lifestyle. Many of the enrolled patients prefer to eat western-type food including Burgers, Pizza and a local delicacy like Biryani and kebab was common among all. History also revealed that most of them could not eat on time either due to work or some other delay. Most of them had habit of chewing paan or having plain betel nut after taking a meal and few had habit of eating flavored betel nut throughout the day and some had them at social events, majority (57%) using less than 5 betel nuts per day. Betel nut chewing was more common among females than in males. All of the enrolled patients had picked up this habit of chewing betel nut from their elders. Over 70% of the diabetic patients in the study were betel nut chewers before their diagnosis, and have continued the habit while undergoing treatment for diabetes of whom the majority (80%) of the patients had poor control of their post prandial blood glucose level which suggests a possible relation between chewing of betel nut after food and poor blood glucose control. A study in the United Kingdom found that weight gain and hyperglycaemia were associated with betel nut chewing among Asians living in east London<sup>22</sup>, and similar studies in Taiwan and Port Moresby, the prevalence of high fasting capillary blood glucose was found to be more than 30% among betel nut chewers compared to 10% in non-chewers<sup>23</sup> and found that betel nut chewing is an independent risk factor for type 2 diabetes mellitus<sup>24</sup>. Adapted to a sedentary lifestyle most of their work included working from a office chair and involved less than 30 minutes of workout. History also revealed that only 20 % of the enrolled members were smokers and many of them only smoked socially. 35 % of them had family history of diabetes with males and females having almost equal distribution.

Many of the diabetic patients were overweight or obese at the time of their diagnosis with males being more obese and Andhra Pradesh ranks 5<sup>th</sup> in the obesity ranking<sup>25</sup>. The association between obesity, physical inactivity and type II diabetes is common among populations in Indians who are obese and physically less active and live in metropolitan cities<sup>26</sup>. Obesity is implicated as an important risk factor as it induces resistance to the action of insulin in type II Diabetes mellitus<sup>27</sup>. The number of insulin receptors on the target cells and/or decreasing glucose transport through post receptor changes may occur in obesity<sup>28</sup>. In view of these research findings, the habit of chewing betel nut by the diabetic patients could help to explain the fact that the majority of them have very poor control of their blood glucose level. This is indicated by the observations that mean post prandial blood glucose levels at the time of diagnosis were slightly lower in non chewers (236,218.1mg/dl) than that of betel nut chewers (270,244.8 mg/dl) in both males and females respectively. There was no significant difference (p>0.001) in the fasting values at the time of diagnosis and values in both males and females showed similar distribution. Post prandial blood glucose levels at three months in non chewers (142.3, 158.6 mg/dl) were significantly lower (P<0.001) than that of betel nut chewers (185, 191 mg/dl) in both males and females respectively. Females showed a better control of post prandial blood glucose than males at 3 months (P< 0.01). The statistical difference was not significant (P>0.001) when fasting blood glucose was compared at 3 months intervals and both males and females had similar distribution of values (P>0.001). HbA1c levels in non chewers (7.2, 7.4) were significantly lower (P<0.001) than betel nut chewers (7.9, 8.3) in both males and females respectively. Female non chewers showed better control with lower mean blood glucose levels (P<0.001). The above results clearly indicate that chewing betel nut has a significant effect on post prandial blood glucose levels and the effect appears to be more prominent in females. It is imperative that patients are involved in their own self-care

management. Counseling programs on physical activity improve blood glucose control in diabetes<sup>29</sup>. There is evidence that adequate patient education improves control of blood glucose level and reduces complications<sup>30</sup>. The patients also need to be informed about the likely harmful effects of betel nut chewing on their diabetes mellitus. In this study, there are possible confounders (that have not been controlled for) such as non-compliance with treatment, change of oral hypoglycemic and choice of oral hypoglycemics and the patients' inappropriate diet including alcohol that would contribute to poor glycaemic control. However, in view of the findings in the present study and other studies, betel nut chewing is likely to be a contributing factor to the poor glycaemic control mostly affecting the post prandial blood glucose levels.

### Conclusion

Betel nut chewing may be a contributing factor to the poor glycaemic control in diabetic patients affecting the post prandial blood glucose levels. As the majority of diabetic patients have poor control of their blood glucose, this observation concerning the effect of betel nut chewing on blood glucose control and its predilection towards females should be made known to the patients, their families and the community because many people chew betel nut but do not know the risks involved in this habit. They should be specifically advised to avoid betel nut chewing after food as this practice may be helpful in better control of post prandial blood glucose and avoidance of large doses of oral hypoglycemics. Diabetes patients' education and training is one of the most important activities in the overall management of diabetes mellitus. It is important for the patients and their families to increase their knowledge, skill and self-management abilities in order for them to make changes in their lifestyle, and enable them to cope with the disease. Good diabetes knowledge with a positive emotional outlook, and understanding of the problems that may occur in the course of the disease, may help the patient to maintain good health. Further investigations involving other confounding factors and other GABA receptor inhibitors should be undertaken to test the link between betel nut chewing and poor glycaemic control.

### References

- Nelson BS, Heischouer B. Betelnut: a common drug used by naturalised citizens from India, Far East Asia, and the South Pacific Islands. *Ann Emerg Med* 1999;34:238± 43.
- CRN India. Analyzing the stock market commodity, areca nut overview. Retrieved from <http://www.crnindia.com/commodity/arecanut.html>
- Norton SA. Betel: consumption and consequences. *J Am Acad Dermatol* 1998;38:81± 8.
- Gupta Prakash Chandra, Ray Cecily S (July 2004). "Epidemiology of betel quid usage". *Ann. Acad. Med. Singap.* 33 (4 Suppl): 31–6.
- Encyclopaedia Britannica. Areca catechu. Betel nut. 1974:c 1877. Encyclopaedia Britannica, 15<sup>th</sup> edn.
- Tillakaratne NJ, Medina-Kauwe L, Gibson KM. Gamma-aminobutyric acid (GABA) metabolism in mammalian neural and non-neural tissues. *Comp Biochem Physiol A Physiol* 1995;112:247 ± 63.
- Scutt A, Meghi S, Harvey W. Stimulation of human fibroblast collagen synthesis in vitro by gammaaminobutyric acid. *Biochem Pharmacol* 1987;36:1333± 5.
- Schousboe A, Thorbek P, Hertz L et al. Effects of GABA analogues of restricted conformation on GABA transport in astrocytes and brain cortex slices and on GABA receptor binding. *J Neurochem* 1979;33:181± 9.
- Deahl M. Betel-induced extrapyramidal syndrome: an unusual drug reaction. *Mov Disord* 1989; 4:330± 2.
- Chu NS. Betel chewing increases the skin temperature: effects of atropine and propranolol. *Neurosci Lett* 1995;194:130 ± 2.
- Chu NS. Cardiovascular responses to betel chewing. *J Formos Med Assoc* 1993;92:835 ± 7.
- Wang CK, Hwang LS. Effect of betel quid on catecholamine secretion from adrenal chromaffin cells. *Proc Natl Sci Repub China B* 1997; 21:129± 36.
- Wang CK, Hwang LS. Effect of betel quid on catecholamine secretion from adrenal chromaffin cells. *Proc Natl Sci Repub China B* 1997; 21:129± 36.

- Martino GV, Tappaz ML, Braghi S et al. Autoantibodies to glutamic acid decarboxylase (GAD) detected by an immuno-trapping enzyme activity assay: relation to insulin-dependent diabetes mellitus and islet cell antibodies. *J Autoimmun* 1991; 4:915± 23.
- Smismans A, Schuit F, Pipeleers D. Nutrient regulation of gamma-butyric acid release from islet beta cells. *Diabetologia* 1997;40:1411± 15.
- Okamoto H, Yanamoto H, Takasawa S et al. Molecular mechanism of degeneration: oncogenesis and regeneration of pancreatic beta-cells of islets of Langerhans. In: Shafir E, Renold AE, editors. *Frontiers in diabetes research lessons from animal*. London: John Libby & Co.; 1988, pp. 149± 57.
39. Dahlquist G Blom L, Persson LA, Sandstrom AI, Wall SG. Dietary factors and the risk of developing insulin dependent diabetes in childhood. *Br Med J* 1990;300:1302 ± 6.
- Boucher BJ, Ewen SWB, Stowers JM. Betelnut (Areca catechu) consumption and the induction of glucose intolerance in adult CD1 mice and their F1 and F2 offspring. *Diabetologia* 1994;37: 49± 55. 110 B. J. Boucher & N. Mannan
- Mannan N, Boucher BJ, Evans SJW. Increased waist size and weight in relation to consumption of Areca catechu (betel-nut); a risk factor for increased glycaemia in Asians in East London. *Br J Nutr* 2000;83:267± 75.
- Who India. Communicable diseases dept. Blood safety and clinical technology. guidelines on standard operating procedures for clinical chemistry. section b: biochemical measurements in plasma and serum.
- Trinder, P. (1969). *Annals of Clin. Biochem.* 6: 24 - 27
- Mannan N, Boucher BJ, Evans SJ. Increased waist size and weight in relation to consumption of Areca catechu ( betel-nut); a risk factor for increased glycemia in Asians in east London. *Br J Nutr* 2000;83:267-275.
- Benjamin AL. Community screening for diabetes in the National Capital District, Papua New Guinea: is betelnut chewing a risk factor for diabetes? *PNG Med J* 2001;44:101-107.
- Tung TH, Chiu YH, Chen LS, Wu HM, Boucher BJ, Chen TH, Keelung Community-based Integrated Screening Programme No. 2. A population-based study of the association between areca nut chewing and type 2 diabetes mellitus in Taiwan. *Diabetologia* 2004;47:1776-1781.
- "National Family Health Survey, 2005-06". *Mumbai: International Institute for Population Sciences.* 2007
- "India facing obesity epidemic: experts". *The Hindu.* 2007-10-12.
- Dowse GK, Zimmet PZ, Gareeboo H, George K, Alberti MM, Tuomilehto J, Finch CF, Chitson P, Tulsidas H. Abdominal obesity and physical inactivity as risk factors for NIDDM and impaired glucose tolerance in Indian, Creole, and Chinese Mauritians. *Diabetes Care* 1991;14:271-282.
- World Health Organization. Diabetes Mellitus. WHO Tech Rep Ser No 727. Geneva: World Health Organization, 1985.
- International Diabetes Federation. *Diabetes Atlas*, 2nd edition. Brussels: IDF, 2003.
- McGill M. Diabetes education: a keystone in the management of diabetes. *PNG Med J* 2001;44:131- 134