Thyroid Disorders in Type 2 Diabetes Mellitus

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Research Article

Abstract: **Background:** Diabetes mellitus and thyroid diseases are the two common endocriniopathies seen with increasing frequencies in the adult population. Thyroid dysfunctions complicate management of diabetes mellitus and its complications. There is little reliable information on the prevalence of hyperthyroidism and hypothyroidism in the community. The incidence of hypothyroidism in different communities has varied from 0,6 % to 1,5 %. **Materials and Methods:** The subjects were selected from the cases presenting with diabetes mellitus (TYPE2) in the OPD and ward of department of medicine for a period of two years from 1-8-2009 to 31-7-2011, in SVS Medical College and Hospital, Mahabubnagar, Andhra Pradesh. . The study population consisted of 200 diabetic and 100 non diabetic subjects. The following investigations done in all the cases – fasting and post-prandial blood sugars, HbA_1C, blood urea, serum Creatinine, serum lipid profile, T3, T4, and TSH. **Observations:** 108 male and 92 female cases were in the study group while 52 male and 48 female constituted the control group. Thyroid function tests were significantly low when compared with that of control group. 8 male diabetics and 18 female diabetic had hypothyroidism as compared to one and 4 in control group. Four male and 4 female diabetics fell into sub-clinical hypothyroidism group; only one control female had sub-clinical hypothyroid status. Two female diabetes patients showed hyperthyroidism; 2 female and 2 male patients exhibited sub-clinical hyperthyroidism while only 2 female had sub-clinical hyperthyroidism. **Discussion:** Forty patients showed abnormal thyroid functions in a study sample of 200 while 8 in control group had abnormal thyroid function. These results were compared to that in earlier literature. Thyroid function tests to be estimated at least once in a year at discretion of treating physician.

Keywords: Diabetes mellitus, thyroid function, management, control of diabetes.

Introduction

Diabetes mellitus and thyroid diseases are the two common endocriniopathies seen with increasing frequencies in the adult population and hyperthyroidism results in deterioration of diabetic control[1]. Patients with hyperthyroidism will show high blood glucose level after meals and hyperthyroidism increases severity of diabetes (hyperglycaemia), probably due to stimulation of the metabolic rate leading to increased lipid and protein catabolism[2]. Thyroid dysfunctions complicate management of diabetes mellitus and its complications[3]. Clinically, thyroid dysfunction may undermine diabetes control. For example, hyperthyroidism may worsen glycaemia control and increase insulin requirements. It is reported[4,5] that, thyroid dysfunction is common in diabetic patients and can produce significant metabolic disturbances such as increased hepatic gluconeogenesis, rapid gastrointestinal glucose absorption, and glucose intolerance**.** Radaideh *et al*[6] recommended that, diabetes mellitus patients should be screened for asymptomatic thyroid dysfunction which is increased in frequency in diabetic population. Glucose intolerance is common in hyperthyroidism[7].

Materials and Method

The subjects were selected from the cases presenting with diabetes mellitus (TYPE2) in the OPD and ward of department of medicine for a period of two years from 1-8-2009 to 31-7-2011, in SVS Medical College and Hospital, Mahabubnagar, Andhra Pradesh. An informed written consent was taken from each and every patient. The study population consisted of 200 diabetic and 100 non diabetic subjects. The criteria for diagnosis of diabetes were the American Diabetic Association criteria; FPG of 110 mg/dl, random blood sugar of 200 mg/dl or taking anti-hyperglycaemic drugs without any episode of diabetic keto-acidosis. All the patients with diseases that may affect thyroid function were excluded. The patients on medications that can affect thyroid function were also excluded. The non diabetes volunteers without history of DM whose FPG were less than 110 mg /dl on two occasions were taken as the control samples. These volunteers included non-diabetic subjects who came in the hospitals for routine checkups as advised by their attending physicians. The controls were not taking any drugs. All three hundred were clinically assessed for any thyromegaly, or any clinical sign of hypo- or hyper-thyroidism. The following investigations done in all the cases – fasting and post-prandial blood sugars, HbA_1C, blood urea, serum Creatinine, serum lipid profile, T3, T4, and TSH. The results of thyroid function tests were analysed and tabulated into one of the 5 categories as follows.

	T3	T4	TSH
Normal	NORMAL (80-200ng/dl)	NORMAL (4.5 – 11.5 ug/dl)	NORMAL (0.3 – 5.0 uIU/dl)
Hypothyroidism	LOW	LOW	HIGH >6uIU/dl
Subclinical hypothroidism	NORMAL	NORMAL	HIGH >6uIU/dl
Hyperthyroidism	HIGH	HIGH	LOW < 0.2 uIU/dl
Subclinical hyperthyroidism	NORMAL	NORMAL	LOW < 0.2 uIU/dl

Statistical Analysis

Quantitative data summarized to test the difference in mean values obtained for NIDDM patients and controls using student't' test, p value < 0.05 is taken as the level of significance. Further, Pearson's correlation was used to correlate between the FSG and thyroid profile.

Observations

Table 1: age and sex of the cases in study and control group

	Number of Cases	Mean Age in Years
DM Male	108	48.88
DM Female	92	48.26
Control Male	52	47.98
Control Female	48	48.04

Table 2: Values of investigations amongst two study groups

Parameter	DM Group	Control Group	'p' Value
FBS (mg/dl)	162.43	89.78	0.0025
PPBS (mg/dl)	198.52	104.6	0.0031
S. TOTAL CHOLESTEROL (mg/dl)	204.56	168.50	0.045
HDL CHOLESTEROL (mg/dl)	30.56	42.68	0.076
LDL CHOLESTEROL (mg/dl)	109.80	86.12	0.056
VLDL CHOLESTEROL (mg/dl)	32.96	26.26	0.064
TRIGLYCERIDES (mg/dl)	168.45	108.65	0.046
BLOOD UREA (mg/dl)	38.44	26.05	0.065
SERUM CREATININE (mg/dl)	1.42	0.94	0.052
HbA_1C (%AGE)	8.20	5.48	0.036
SGOT (U/L)	44.06	28.58	0.058
SGPT(U/L)	48.06	21.08	0.045
SERUM TOTAL PROTEIN (G/dl)	6.98	7.68	0.062
SERUM ALBUMIN (G/dl)	3.88	4.02	0.068
SERUM GLOBULIN (G/dl)	3.10	3.66	0.072

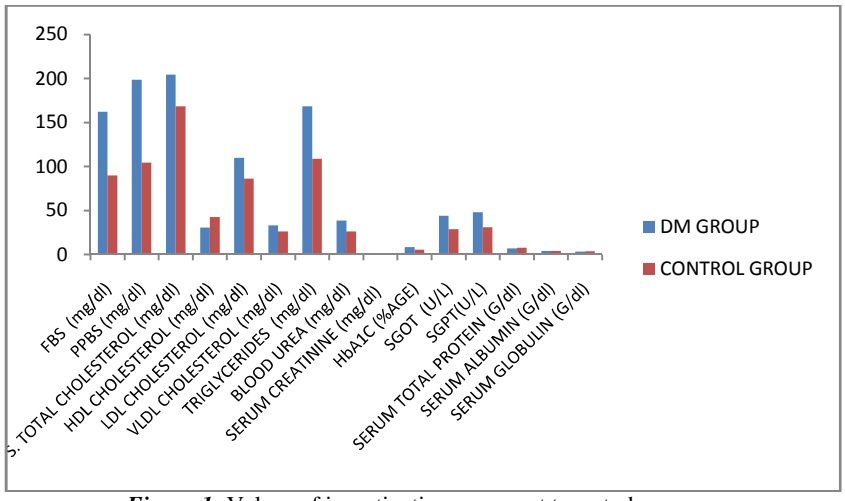

Figure 1: Values of investigations amongst two study groups

Table 3: Showing Comparission of Mean Thyroid Function Tests in DM and Control Groups

Investigation	DM Group	Control Group	'p' Value
T 3 (ng/dl)	114.56	168.45	< 0.001
T 4 (ug/dl)	6.98	10.46	<0.001

TSH (uIU/dl)	6.04	2.84	<0.001

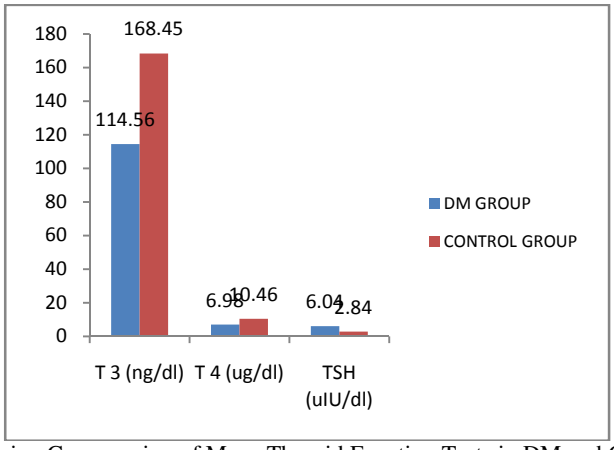

Figure 2: Showing Compression of Mean Thyroid Function Tests in DM and Control Groups

Table 4: Showing Number of Patients Various Thyroid Disorders Detected in Our Study

	Hypothyroidism	**Subclinical hypothyroidism**	**Hyperthyroidism**	**Sub-clinical hyperthyoidism**
Dm male	8	4	0	2
Dm female	18	4	2	2
Control male	1	0	0	0
Control female	4	1	0	2

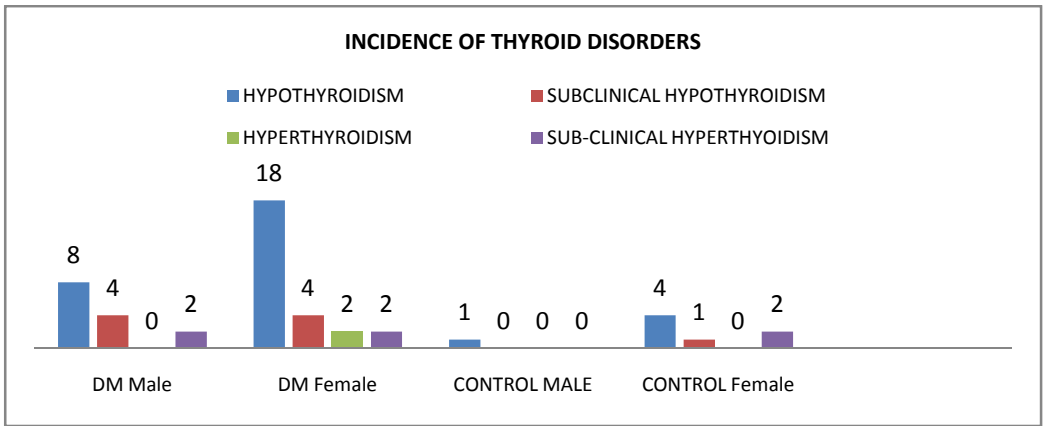

Figure 3: Showing Number of Patients Various Thyroid Disorders Detected in Our Study

One female patient who was diagnosed as T2 DM 4 years ago presented with goiter, and she showed sub-clinical hypothyroidism.

Table 5: Showing Number of Patients with Thyroid Function Abnormalities

	DM GROUP	**COTROL GROUP**	**'p' Value**
MALE	14	1	< 0.001
FEMALE	26	7	< 0.001
TOTAL	40	8	< 0.001

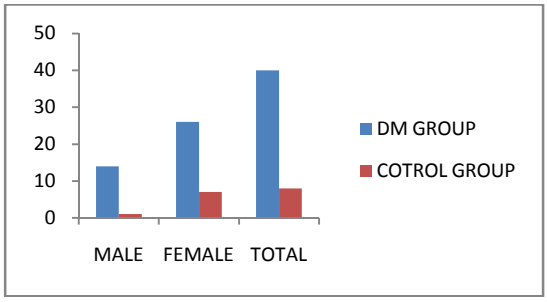

Figure 4: Showing Number of Patients with Thyroid Function Abnormalities

Table 6: Showing the Incidence of Hypothyroidism Vs Hyperthyroidism

	Hypothyroidism	**Hyperthyroidism**	**'p' value**
DM group male	12	2	< 0.001
DM group female	22	4	< 0.001
Control male	1	0	< 0.001
Control female	5	2	0.056

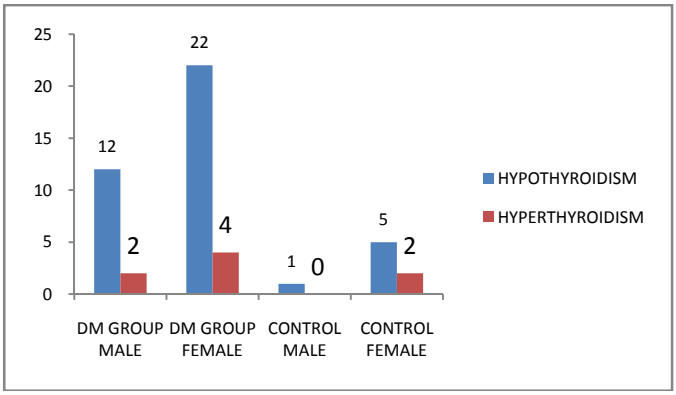

Figure 5: Showing the Incidence of Hypothyroidism Vs Hyperthyroidism

Discussion

Forty patients showed abnormal thyroid functions in a study sample of 200 while 8 in control group had abnormal thyroid function. There is little reliable information on the prevalence of hyperthyroidism and hypothyroidism in the community. The incidence of hypothyroidism in different communities has varied from 0,6 % to 1,5 % [8]. Thyroid hormones are insulin antagonists, both insulin and thyroid hormones are involved in cellular metabolism and excess and deficit of any one can result in functional derangement of the other [9]. Thyroid disease is a pathological state that adversely affects diabetic control and is commonly found in most forms of DM which is associated with advanced age in type 2 diabetes and autoimmune diseases in type 1diabetes. DM appears to influence thyroid function in two sites; firstly at the level of hypothalamic control of TSH release and secondly at the conversion of T4 to T3 in the peripheral tissue. Marked hyperglycemia causes reversible reduction of the activity and hepatic concentration of T4-5-deiodinase, low serum concentration of T3, elevated levels of reverse T3 and low, normal, or high level of T4 [10]. A variety of thyroid abnormalities may co-exist and interact with diabetes mellitus. The reported frequency of hyperthyroidism and hypothyroidism in patients with diabetes has varied from 3.2 % to 4.6 % and 0.7 % to 4.0 % respectively [8]. As early as 1968 it was reported that there exists the association of hypothyroidism in diabetic patients [11]. Later studies in 1979 emphasized the importance of screening of diabetic patients to identify hypothyroidism [6, 12]. Now it has been found that thyroid disease and both type 1 and type 2 diabetes mellitus are strongly associated and this has important clinical implications for treatment requirements[13]. Also, diabetes mellitus patients with hypothyroidism are at increased risk for complications like nephropathy. In our study it was found that the prevalence of hypothyroidism was 12.06 % which is in accordance with the studies of Perros *et al*[14]. (13.4%) and Papazafiropoulou (12.3%)[15]. This study also identified the atrisk group with subclinical hypothyroidism. The number of diabetes mellitus patients with subclinical hypothyroidism was found to be 18 (31.03%). These significant percentages emphasize that the diabetic patients to be followed up with thyroid profile. In order to assess the trend this study compared the mean values of thyroid profile between controls and diabetics. It was found that the diabetics showed the trend towards the hypothyroidism. The pathophysiology of thyroid dysfunction in diabetes is still unclear; however thyroid antibodies have been suggested to be the causative factors [16]. Yet to be published review reveals that the cause may be due to the complex interaction of common signaling pathways of insulin modulation and feedback mechanism of thyroid hormones [17]. This study did not show any correlation between fasting sugar levels and parameters of thyroid profile. This may suggests that absence or minimal role of blood sugar concentration in thyroid dysfunction and further studies with glycated hemoglobin may be necessary to find the role of glycemic status in causing thyroid dysfunction. The limitation of this study is, it's a cross sectional study with lesser sample size and hence a follow up study may be required to substantiate the findings. With this study it can be concluded that

diabetics are at increased risk for hypothyroidism and their FSG levels do not predict the risk.

Table 7: Showing Thyroid Morphology Compared to Available Studies

Thyroid morphology	**Engine *et al* (1999)** [18] [in percentage]	**Mazin Z Al-Shibani (2010)** [19] [in percentage]	Present study [in percentage]
Normal		83.13	
Diffuse goiter	4.5	5.3	
Solitary nodule	2.9	6.02	0.5
MNG	5	4.1	
THYROIDECTOMY		1.45	

Table 8: Showing Various Sub-Types of Thyroid Disorders as Compared With Earlier Studies

	Engin *et al* [18]	**Radaideh *et al*** [6] **2004**	**Udiong** [20] **2007**	**Pasupathi *et al*** [21] **2008**	**Mazin Z Al-Shibani**[19] **2010**	Saha *et al* [22] 2010	Oromcan *et al* [23] 2010	G Singh *et al* [24] 2011	Swamy RM *et al* [25] 2012	Present study
Sub-clinical Hypothyroidism				5.1	6.8	5	1.8	15	31.03	4
Hypothyroidism	1.1	8.9	26.6	3.8	4.1	6.66	1.8	9	12.06	13
Sub-clinical Hyperthyroidism					3.1	6.66	0.9	0		2
Hyperthyroidism	1.3		19.8		4.3	20	3.5	9.25		1
SES					5.3			-		-
Euthyroid					76.4		86.8	66.75		80

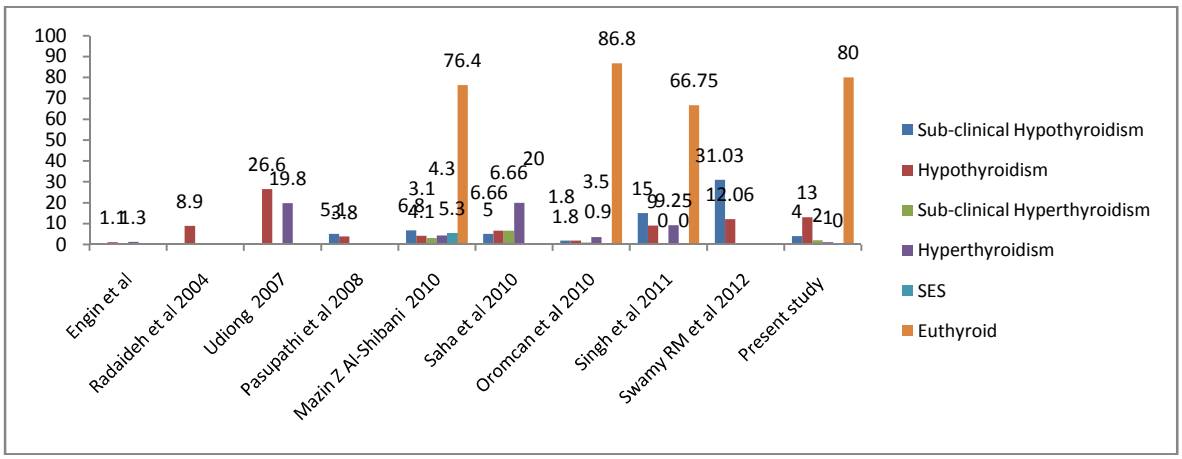

Figure 6: Showing Various Sub-Types of Thyroid Disorders as Compared With Earlier Studies

There has been substantial evidence in the abnormal thyroid function tests both from the present study and that from literature particularly hypothyroidism in type 2 diabete mellitus patients. Finally, whether all patients with diabetes should be screened for thyroid function or whether patients with subclinical thyroid disease should be treated merits reconsideration.

Conflicts

The authors declare none in this study

References

1. Sathish, R., Mohan, V. 2003. Diabetes and Thyroid Diseases - A Review. Int. J. Diab. Dev. Countries. 23: 121.
2. Rafelson, M.E., Hayashi, J.A., Bezkorovainy, A. 1980. Basic biochemistry, 4th ed. USA, Macmillan Publishing Co., Inc.
3. Greener, M. 2000. Thyroid disease and diabetes. A DG Review of: "Practical Pointers: Thyroid Disease and Diabetes". Clinical Diabetes. [Internet]. Available at: http://www.ithyroid.com/idiabetes.htm [Accessed 10 November 2007].
4. Wu, P. 2000. Practical pointers: Thyroid disease and diabetes. Clinical diabetes. 18(1).

5. Klieverik, L.P., Sauerwein, H.P., Ackermans, M.T., Boelen, A., Kalsbeek, A., Fliers, E. 2008. Effects of thyrotoxicosis and selective hepatic autonomic denervation on hepatic sglucose metabolism in rats. . Am J Physiol Endocrinol Metab. 294 (3): E513-20. Epub 2008 Jan 8.
6. Radaideh, A.R., Nusier, M.K., Amari, F.L., Bateiha, A.E., El- Khateeb, M.S., Naser, A.S., Ajlouni, K.M. 2004. Thyroid dysfunction in patients with type 2 diabetes mellitus in Jordan. Saudi Med J. 25(8):1046-50.
7. Roubsanthisuk, W., Watanakejorn, P., Tunlakit, M., Sriussadaporn, S. 2006. Hyperthyroidism induces glucose intolerance by lowering both insulin secretion and peripheral insulin sensitivity. J Med Assoc Thai. 89 Suppl 5:S133-40.
8. J. Feely and T. E. Isles, "Screening for thyroid dysfunction in diabetics," British Medical Journal, vol. 1, no. 6179, p. 1678, 1979.
9. Sugure, D.D., Mc Evoy, M. and Drury, M.I.(1999). Thyroid disease in diabetics. Postgrad Med J. 680-684.
10. Shah SN. Thyroid disease in diabetes mellitus. J Assoc Physicians India; 1998:32(12): 1057-1059.
11. D. H. Akbar, M. M. Ahmed, and J. Al-Mughales, "Thyroid dysfunction and thyroid autoimmunity in Saudi type 2 diabetics," Acta Diabetologica, vol. 43, no. 1, pp. 14–18, 2006.
12. O. Kordonouri, N. Charpentier, and R. Hartmann, "GADA positivity at onset of type 1 diabetes is a risk factor for the development of autoimmune thyroiditis," Pediatric Diabetes, vol. 12, no. 1, pp. 31–33, 2011.
13. G. Radetti, C. Paganini, L. Gentill et al., "Frequency of Hashimoto's thyroiditis in children with type 1 diabetes mellitus," Acta Diabetologica, vol. 32, no. 2, pp. 121–124, 1995.
14. P. Perros, R. J. McCrimmon, G. Shaw, and B. M. Frier, "Frequency of thyroid dysfunction in diabetic patients: value of annual screening," DiabeticMedicine, vol. 12, no. 7, pp. 622– 627, 1995.
15. A. Papazafiropoulou, "Prevalence of thyroid dysfunction among greek Type 2 diabetic patients attending an outpatient clinic," Journal of Clinical Medicine Research, vol. 2, no. 2, pp. 75–78, 2010.
16. O. Kordonouri, D. Deiss, T. Danne, A. Dorow, C. Bassir, and A. Gr¨uters-Kieslich, "Predictivity of thyroid autoantibodies for the development of thyroid disorders in children and adolescents with Type 1 diabetes," Diabetic Medicine, vol. 19, no. 6, pp. 518–521, 2002.
17. J. G. Hollowell, N. W. Staehling, W. Dana Flanders et al., "Serum TSH, T4, and thyroid antibodies in the United States population (1988 to 1994): National Health and Nutrition Examination Survey (NHANES III)," Journal of Clinical Endocrinology and Metabolism, vol. 87, no. 2, pp. 489–499, 2002.
18. Engin G.ney, Belgin Efe, Aysen AkalÝn, Nur Kebap Ý, Esat ErenoÛlu, Thyroid Disease in Diabetes Mellitus Turkish Journal of Endocrinology and Metabolism, (1999) 3 : 119-122
19. Mazin Z Al-Shibani Diabetes Mellitus and Thyroid Disorders Kufa Med Journal 2010.VOL.13.No.1: 60-67
20. C. E.J. Udiong, A., E. Udoh and M. E. Etukudoh Evaluation of Thyroid Function in Diabetes Mellitus in Calabar, Nigeria Indian Journal of Clinical Biochemistry, 2007 / 22 (2) 74-78
21. Palanisamy Pasupathi, Govindaswamy. Bakthavathsalam, Ganesan Saravanan, Ramachandran Sundaramoorthi Screening for Thyroid Dysfunction in the Diabetic/Non-Diabetic Population Thyroid Science 3(8):CLS1-6, 2008 www.ThyroidScience.com Clinical and Lab Studies
22. Saha HR, Sarkar BC, Khan SA, Sana NK, Choudhury S (2012) A Comparative Study of Thyroid Hormone and Lipid Status in Diabetic and Non Diabetic Adults. 1:450. doi:10.4172/scientificreports.450 2-5
23. B.W. Oromcan and S. Okello Thyroid function among diabetic patients at Mengo Hospital Kampala Africa Journal of Animal and Biomedical Sciences 5 (1), 2010 42-55
24. Gurjeet Singh, Vikas Gupta, Anu Kumar Sharma and Neeraj Gupta: Frequency of Thyroid Dysfunction Among Diabetes in Punjabi Population
Biological Forum — An International Journal, 3(1): 74-77(2011)
25. Swamy RM, Naveen Kumar, Srinivasa K, Manjunath GN, Prasad Byrav DS, Venkatesh G., Evaluation of hypothyroidism as a complication in Type II Diabetes Mellitus Biomedical Research 2012; 23 (2): 170-172.