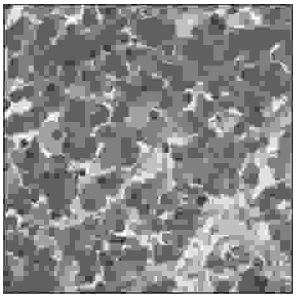
ORIGINAL PROF-912

NODULAR GOITERS



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ABSTRACT… Objective: The purpose of the study was to estimate the levels of amino sugars and glycosylated proteins in the blood and thyroid tissues of the patients suffering from thyroid disorders. **Study design:** The study was carried out at Basic Medical sciences Institute, J.P.M.C. Karachi. **Period:** From 1990 to 1992. **Materials & Methods:** Twenty control subjects and 35 thyroid patients (Non toxic goiter = 14, Non toxic nodular goiter = 12 and Toxic nodular goiter=9) were studied. T_4, TBG and T_4/TBG ratio, serum and tissue glucose, protein, glycosylated proteins and hexosamine with their correlation coefficient (r) were estimated **Results:** Significantly raised levels of TBG in non toxic goiter and toxic nodular goiter while T_4/TBG ratio was significantly decreased in non toxic goiter and toxic nodular goiter. In non toxic goiter patients correlation coefficient analysis showed a direct relationship (serum to tissue levels) of glucose(r=0.47), glycosylated proteins(r=0.40) and hexosamine (r=0.23) while an inverse relationship was found in case of protein(r= -0.38). In non toxic nodular group inverse relationship was only found in proteins (r= -0.48) estimation while direct correlation coefficient was observed in glucose (r= 0.29), glycosylated proteins (r=0.13) and in hexosamine (r=0.14). In toxic nodular group hexosamine shows a direct correlation coefficient(r=0.73)while glucose (= -0.53), proteins (r= -0.87)and glycosylated proteins(r= -0.12) have an inverse relationship. **Conclusion:** It was concluded from correlation coefficient analysis (blood to tissue levels) that in non toxic goiter and non toxic nodular patients glucose, glycosylated protein and hexosamine showed a direct relationship while protein showed an inverse relationship.

INTRODUCTION

The major constituent of colloid is a large glycoprotein, the thyroglobulin which comprises about 70-80% of the thyroid gland protein[2]. Winzler et al[3] classified the carbohydrate containing proteins into two major groups, the glycoproteins and mucoproteins. Glycoproteins may be defined as the proteins which have carbohydrate moieties covalently linked to the peptide chain. Interest in glycoprotein has been stimulated by their physiological as well as by their involvement in a variety of pathological states. The association of serum glycoproteins and mucoproteins with cancer[4]and other pathological conditions was known long before their characterization was done[5]. Total protein bound carbohydrates in normal serum and its variations in diseases like tuberculosis, sub-acute bacterial endo carditis, advanced cancer[6] and parenchymatous liver diseases, Hashimoto's disease[7] was further investigated by Winzler et al[3] and reported that average values of the total protein bound carbohydrates in serum of normal person is 273.3mg%, with 121.0 mg% protein bound hexoses, 83.4mg% hexosamine, 8.9mg%, fucose and

60.0 mg% sialic acid. Several sugar characteristics of glycoproteins have been shown to be present in this molecule and analysis for some of these have been reported[8,9]. Proteins containing carbohydrate are widely distributed in animal tissues and include such diverse compounds as blood group substances, serum proteins, mucin, pituitary hormones and connective tissue elements.

The biological properties of glycoproteins depend upon the nature and amount of carbohydrate prosthetic group along with polypeptide chain[10] The biological role of carbohydrate group is stabilization of proteins, specification of human blood groups and their ability to recognize and bind selectively to other cells or to soluble molecules such as hormones. There is also an evidence that carbohydrate is involved in stabilization of glycoproteins during passage from the rough endoplasmic reticulum to the cell surface and in recognition phenomenon such as receptor mediated endocytosis as the oligosaccharides have relatively rigid structures, routing of lysosomal hydrolases to the lysosome and in the spread of cancer cells to secondary sites. There is evidence that oncogenic transformation[11] is associated with increased size cell surface carbohydrate[12]. These glycoproteins are those proteins which contain more than 0.5% hexosamine which is firmly bound and can be hydrolyzed by an alkali, acid or enzyme.

The thyroid gland is composed of large number of closed follicles filled with colloid material and lined with cuboidal epitheloid cells. The major constituent of colloid is a large glycoprotein, the thyroid globulin i.e. 19-s iodoglycoprotien, which contain thyroid hormones, mainly thyroxine and triiodothyronine, Spiro[13] studied the thyroglobulin of sheep, calf, pig and human and showed that thyroglobulin is a high molecular weight (660,000) glycoprotein which has been shown to contain approximately 300 monosaccharide residues per molecule in the form of galactose, mannose, glucosamine, sialic acid and fucose etc. Extensive variations in thyroglobulin structure are frequently associated with goiter and these may be involved in pathogenesis[14]. Refetoff et al[15] also studied the physical, chemical and biological properties of radio iodinated Thyroxine Binding Globulin TBG and partially desialylated or slow desialylated STBG, preserve their biological and immunologic properties, they are useful as tracer material for metabolic studies. Conversion of thyroglobulin to Sialyated Thyroxine Binding Globulin (STBG) may be limiting step in the regulation of TBG metabolism. It was suggested by Riesco et al[16] that an impairment in the amount of thyroglobulin available for iodination could be the underlying defect leading to the presence in thyroid and serum, of abnormal iodinated compounds and to defective coupling. Thyroxine and triiodothyronine are the only physiologically active hormones[17].

The pathogenesis of goiter involves hypertrophy and hyperplasia of thyroid follicular cells by elevated levels of TSH[18]. In most cases, such changes result initially in diffuse, symmetric enlargement of the gland (diffuse non toxic goiter). The follicles are lined by crowded columnar cells, which may pile up and from projections similar to those seen in Grave's disease[19]. If dietary iodine subsequently increases, or if the demands for thyroid hormone decrease, the stimulated follicular epithelium involutes to form, an enlarged, colloid-rich gland (colloid goiter). Colloid is abundant during the later periods. With time, recurrent episodes of stimulation and involution combine to produce a more irregular enlargement of the thyroid, termed nodular, or multi-nodular goiter. The basis of nodule formation is not clear. It may be related to differential ability of normal thyroid epithelial cells to replicate in response to TSH. Conceivably, this variation in cell growth potential can cause nodular formation with cyclical and long-term exposure to increased levels of TSH[20.] Hormone production in functional adenomas. occurs independent of TSH stimulation; hence they are called "autonomous nodules"[20.] Recent genetic analysis have shown that toxic adenomas often harbour activating mutations of either the TSH receptor gene called GNASI. GNASI encodes the a-subunit of the hetero dimeric protein G_s[21] . Normally, the binding of TSH to its receptor activates $G_{sa'}$ which in turn leads to up-regulation of adenyl cyclase and its product cyclic AMP. One of the

endpoints of this tightly regulated cascade is increased transcription of thyroid hormones. In the presence of mutations that constitutively activate either the TSH receptor or the G_{sa} protein, there is continuous thyroid hormone production and hyperthyroidism even in the absence of TSH stimulation. The study was planned to find out the role of aminosugars (hexosamine)and proteins (glycosylated)in the pathogenesis of thyroid toxicity and its conversion into nodular and then into cancerous form later on.

MATERIALS AND METHODS

Patients

Patients suffering from thyroid disorders, admitted in Surgical Units of Jinah Postgraduate Medical Centre, Surgical Units and ENT wards of Civil Hospital Karachi were selected. Diagnosis of the patients was carried out on the basis of history of patients, physical examination and radioisotopic studies such as Thyroid scanning and Isotopic iodine uptake.

Control Subjects

Age matched subjects having no history of thyroid disease were selected from normal population. Most of the normal subjects were selected from amongst the students and staff members of Basic Medical Sciences Institute, J.P.M.C. Karachi.

Blood Collection

Fifteen to twenty ml of blood was collected from each patient by venepuncture. About 5 ml of blood was transferred into a clean centrifuge tube containing a mixture of sodium fluoride and potassium oxalate in a ratio 1:3 as an anticoagulant. Remaining blood was transferred to a dry centrifuge tube. Plasma was separated by centrifugation after 30 minutes of collection of blood and serum after complete coagulation of blood, approximately within one hour of blood collection .Plasma and serum after separation were transferred into dry glass bottles with plastic stoppers.0.5 ml of serum was stored into a plastic container for hormone analysis All the samples were stored in the freezer at -20^{0}C. Before analysis, samples were allowed to attain room temperature. Sialic acid and mucoproteins were estimated by Natelson[22,23] methods respectively.

Thyroid Tissue Collection

Fresh human thyroid tissue was obtained at the time of operation and preserved in ice cold tris-hydrochloric acid buffer at pH 7.5The tissue was dried on filter paper. Adherent fascia and fibrous tissue was removed. The tissue was weighed, minced and chopped Homogenate 20% was prepared in 0.2m Tris- hydrochloric acid buffer (hydroxymethyl- aminomethane 99.0-99.5% of Sigma Chemical Company, USA) at pH 7.5 with Aloe homogenizer (Aloe Scientific company, USA The homogenate was centrifuged at 1500* g for 15 minutes at 4^0 C in a refrigerating centrifuge. It was labeled and stored at 4^0 C in a refrigerator.

RESULT

The results are summarized in Table I-VI mean ± SEM. of each is shown. Twenty apparently healthy normal subjects and 35 patients suffering from thyroid diseases were studied. The cases were divided into three groups namely non toxic goiter(14), non toxic nodular goiter (12) and toxic nodular goiter (9).

Mean values of physical findings i.e. body temperature, blood pressure(systolic and diastolic)and pulse rate in different groups are shown in table-I. The mean levels of body temperature expressed in clinically euthyroid subjects i.e. controls is (36.87).,non toxic goiter (36.83) and toxic nodular goiter (36.87)were remarkably similar. In non toxic goiter patients, the mean level of body temperature (36.75, $p<0.001$) was significantly decreased as compared with control group. The mean levels of systolic blood pressure mm Hg in non toxic nodular goiter group (114.58) was similar to the mean levels of control subjects (109.90). The mean levels of systolic blood pressure in non toxic goiter (122.21, $p<0.001$)and in toxic nodular goiter (150.55, $p<0.001$) is significantly increased. The mean values of pulse rate observed in control subjects (74.50) and in non toxic goiter (74,42) were remarkably similar.

Table-I. Physical findings of patients with control subjects.				
The number or units given in parenthesis. The values are mean ± SEM.				
Group	Temperature C_o	Blood pressure		Pulse rate
		Systolic (mm Hg)	Diastolic (mm Hg)	
Control (20)	36.87±0.02	109.90±1.73	73.95±1.05	74.95±0.41
Non toxic goiter(14)	**36.75±0.02	**122.21±1.95	75.42±1.01	-
Non toxic nodular goiter(12)	36.83±0.02	114.58±3.39	74.58±1.56	75.83±1.42
Toxic nodular goiter (9)	36.87±0.02	**150.55±4.67	-	107.55±1.49
*p< 0.01 as compared with normal control subjects. **p< 0.001 as compared with normal control subjects.				

Mean values of serumT_4, TBG and T_4/TBG quotient are shown in Table-II. The mean levels of T_4 expressed in µg/dl observed in controls (8.17), non toxic goiter (7.57) were similar. The mean levels of T_4 in non toxic nodular goiter (11.45) is slightly higher but was not statistically significant as compared with control group. The mean levels of TBG expressed as µg /ml in control subjects were (13.61). The significant increase was observed in non toxic goiter (34.88, p.<0.001), in toxic nodular goiter patients (39.47, p<0.001) was observed.T_4/TBG ratio was also significantly decreased in non toxic goiter (2.16, p<0.001) and in toxic nodular goiter patients (2.11, p<0.001). In non toxic nodular goiter patients the mean levels were similar to control subjects .

Table- II. Variations of Thyroxine(T_4), Thyroglobulin(TBG), and T_4/TBG quotient in controls and patients. The number of patients or units are given in parenthesis. The values are mean ± SEM			
Group (µg/dl)	T4(µg/ml)	TBG (µg/ml)	TBG & T4/TBG Quotients
Control (20)	8.17±0.41	13.61±0.72	6.29±0.48
Non toxic goiter(14)	7.57±1.17	34.88±1.16***	2.16±6.53***
Non toxic nodular goiter(12)	11.45±2.09	12.68±1.20	10.60±2.99
Toxic nodular goiter (9)	769±0.77	39.47±1.19***	2.11±029***
*p< 0.05, 0.02 as compared with normal control subjects. **p<0.01 as compared with normal control subjects. ***p<0.001 as compared with normal control subjects.			

The mean levels of fasting glucose expressed in mg/dl in control subjects and patients are shown in Table-III. In this study the mean levels of plasma glucose of control subjects (78.29) and non toxic goiter group (95.24) was within normal range.

The levels are significantly increased in toxic nodular goiter patients (97.15, P, 0.05). The values are similar to those of Perveen and Menahan and Wieland who proposed that thyroid hormone enhance the hepatic synthesis of glucose. The possible mechanism appear to involve induction of the hepatic mitochondrial enzyme pyruvate carboxylase and cytosolic enzyme phosphoenol pyruvate carboxykinase. These enzymes are responsible for catalyzing the initial reaction of gluconeogenesis from pyruvate. It has also been observed by Elrick et al[20] that thyroid hormones have a hyperglycaemic effect by two mechanisms. The most important role of T_4 in

carbohydrate metabolism is to increase the absorption of glucose from gastrointestinal tract. It also increases the gluconeogenesis. Mean levels of tissue glucose expressed in mg/100 g of tissues, in non toxic goiter (360.60) and toxic nodular goiter (640.08) are shown in

Table-III Dumont[21] observed the tissue glucose contents and found increased levels in metabolically highly active tissue and correlated this with the degree of hyperplasia of these glands so the higher level of the tissue glucose may be involved in the thyroid pathogenesis. The correlation coefficient analysis between blood glucose and tissue glucose shown a direct relation (i.e when glucose concentration in tissue increase its concentration in blood will also increase), in non toxic goiter patients (r=0.47 P.N.S) and in non toxic nodular goiter group (r=0.29, P.N.S). Inverse relationship was seen in toxic nodular goiter (r= -0.53.p< 0.1) as compared with blood glucose to tissues glucose levels.

Table- III. Variations of glucose in blood and thyroid tissue with its correlation coefficient

Group	Glucose (mg/dl)	Glucose mg/100gm of tissue	Correlation coefficient r
Control (20)	78.29±3.56	-	-
Non toxic goiter (14)	95.24±7.55	360.60±36.65	0.47
Non toxic nodular goiter (12)	64.11±4.69*	580.51±21.46	0.29
Toxic nodular goiter (9)	97.15±5.91*	640.08±46.65	-0.53

**P<0.05, 0.02 as compared with normal control subjects. **P<0.01 as compared with normal control subjects. ***P<0.001 as compared with normal control subjects.*

The mean levels of plasma protein expressed as gm/dl observed in control subject (7.30), non toxic goiter (6.13), non toxic nodular goiter (6.17) and toxic nodular goiter (8.75) were statistically similar and are shown in (Table-IV). The results of this study are in agreement to those of Perveen[19] and Graninger et al[15]. The possible reason may be that thyroid hormones have no effect on the hepatically synthesized proteins e.g. albumin, thyroxine binding globulin and prealbumin etc but have increased on the endothelium associated protein e.g. fibronectin F, VIII etc. The mean levels of tissue proteins expressed as g/100 g of tissue in non toxic goiter (31.94), non toxic nodular goiter (30.06), and in toxic nodular goiter group (29.00) are shown in Table-IV.

On correlation coefficient analysis of plasma protein to tissues protein, an inverse relationship was observed in non toxic goiter (r= -0.38, p<0.01), in non toxic nodular goiter (r=-0.48, P. N.P) and in toxic nodular goiter (r=-0.87, p<0.001).

Table-V shows the mean levels of plasma glycosylated proteins expressed/gram of protein were observed in control subjects (7.11) and non toxic nodular goiter (6.81) were similar but in toxic nodular goiter (8.03, p<0.01) were statistically significant .The results are in agreement with those of Perveen[19]. The mean levels of tissue glycosylated protein in non toxic goiter (13.21), non toxic nodular goiter group (13.70) were observed.. It was observed that glycosylation of proteins is particularly important in the maintenance of integrity of plasma membrane and in facilitating the secretion of protein into extra cellular space[23]. Increased glycosylation was found in diabetes mellitus and the increase is directly related to increase in blood glucose levels[24] The results of controls in this study are in agreement with Merelyn and Naughton et al[24] and Perveen[19]. There was a significant increase in glycosylated plasma protein in toxic nodular goiter (8.03, p<0.01) which are best correlated with significant increase in plasma glucose in these groups. Correlation coefficient analysis showed a direct relationship of ;plasma glycosylated protein to tissue

glycosylated protein in non toxic goiter (r =0.40,p<0.1), non toxic nodular goiter(r =0.13, P.N.S) . An inverse relationship was observed in toxic nodular goiter group (r= -0.12, PNS).

Table- IV. Variations of proteins in serum and thyroid tissue with it correlation coefficient			
Group	**Protein (mg/dl)**	**Protein mg/100gm of tissue**	**Correlation coefficient r**
Control (20)	7.30 ± 0.52	-	-
Non toxic goiter (14)	6.13 ± 0.33	31.94 ± 2.87	-0.38
Non toxic nodular goiter (12)	6.17 ± 0.63	30.06 ± 2.72	-0.48
Toxic nodular goiter (9)	8.75 ± 0.77	29.00 ± 5.07	-0.87

Table-V. Variations of glycosylated protein in serum and thyroid tissue with its correlation coefficients.			
Group	**glycosylated Protein (mg/dl)**	**glycosylated Protein mg/100gm of tissue**	**Correlation coefficient r**
Control (20)	7.11 ± 0.16	-	-
Non toxic goiter (14)	6.51 ± 0.17*	13.21±0.69	0.40
Non toxic nodular goiter (12)	6.81 ± 0.17	12.75±0.91	0.13
Toxic nodular goiter (9)	8.03 ± 0.21**	13.70±0.79	-0.12
**p<0.05, 0.02 as compared with normal control subjects. **p<0.001 as compared with normal control subjects.*			

The mean levels of serum hexsosamine expressed in mg/dl. observed in control (58.73),. in non toxic group (97.51, P<0.001), non toxic nodular goiter (99.69, P<0.001) and toxic nodular goiter (120.75, P<0.001), the mean levels were significantly higher than control group. Hexosamine contents were estimated to find the variation of aminosugar concentration. Carbohydrates in the thyroglobulin exist in two types of units. One consisting of only mannose, N-acetyl glucosamine (unit A). The other is made up of mannose, N acetyl glucosamine, glactose, fucose and sialic acid residue (unit B)[28,34]. These observations indicate that the concentration of unit A carbohydrate in the non toxic goiter may be more than the toxic nodular goiter[7]. Yamammoto et al[33] observed that the contents of unit A of carbohydrates is decreased with increase in thyroid hormone because unit A appears as an intermediate part.

This study was also in agreement to that of Perveen[19]. Mean values of tissues hexosamine expressed in mg/100 gm of tissue are shown in table 6. Mean levels observed in non toxic (522.17), non toxic nodular goiter (855.10), and in toxic nodular goiter (777.86) are shown in this table. Correlation coefficient showed the direct relationship of serum hexosamine to tissue hexosamine in non toxic goiter (r=0.23, P.N.S), non toxic nodular goiter (r= 0.14, PN.S) and toxic nodular goiter (r=0.73, P<0.02).

DISCUSSION

Thyroid tissue is mainly composed of colloid material, the major constituents of the colloid is a large glycoprotein, the thyroglobulin (70-80%). Extensive variation in thyroglobulin are frequently found in patients with goiter which may be involved in pathogenesis and its conversion into cancerous form later on. Elevation of serum glycoprotein may arise as a result of the

depolymerization of the ground substance of the connective tissue with the release of solubolized components into the circulation either in the tissue destructive processes e.g. inflammation, destructive diseases, carcinoma etc. or in tissue proliferative processes e.g. prostatic hyperplasia, pregnancy, blood loss. Winzlar[3] observed significant increase in hexosamine, sialic acid, fucose and mucoproteins in advance cancer, acute tuberculosis, sub-acute bacterial endocarditis and parenchymatous liver diseases. It was also found that various fractions of glycoprotein were increased in serum in different thyroid disorders, urinary stone formers and diabetics It has also been observed byWade[24] that in cancer[25] diagnosis if serum thyroglobulin level is below 50 µg/ml residual tumour deposits are probably present and if level is above 50 µg/ml secondary deposits are invariably present In the light of the pathogenesis of different thyroid disorders[26], it would be interesting to find the tissue glycoprotein variations simultaneously with estimation of these in the blood. No work was conducted to observe the influence of blood glycoprotein and tissue glycoprotein in different thyroid diseases simultaneously.

Table-VI. Variations of hexosamine in blood and thyroid tissue with its correlation coefficient.

Group	Hexosamine (mg/dl)	Hexosamine mg/100gm of tissue	Correlation coefficient r
Control (20)	58.73±3.74	-	-
Non toxic goiter (14)	97.51±.94**	522.7±57.45	0.23
Non toxic nodular goiter (12)	99.69±7.98**	855.10±62.94	0.14
Toxic nodular goiter (9)	120.75±15.99**	777.86±80.24	0.73

***p<0.001 as compared with normal control subjects.*

The study was planned and conducted to document the relationship of serum glycoprotein fractions, glucose, proteins, glycosylated proteins and hexosamine in the thyroid tissue of same group of patients. For this purpose 35 thyroid patients are divided into three groups non toxic goiter, non toxic nodular goiter and toxic nodular goiter. The functional status of the thyroid gland can be assessed by the measurement of serum levels of thyroid hormones. The patients were grouped based on clinical and physical examination and on the serum thyroxine level. Mean thyroxine level of control subject was found to be 8.17 mg/dl, while increased levels of thyroxine were found in non toxic nodular goiter and the decreased levels were observed in non toxic goiter and toxic nodular goiter group[27].

Thyroid hormones increases metabolism in the tissue and causes more rapid utilization of oxygen, cardiac output and heart rate[28]. Thyroid hormone probably has direct effect on the excitability of heart which in turn increases heart rate[29].These effects were also observed by [30] that thyroid hormone augments the contractile state of isolated cardiac preparations by mechanism thought not to involve catacholamines. Pulse rate was significantly increased in toxic nodular goiter (107.55,p<0.001) but some discrepancies were observed compared with control group. The result are in accordance with[31],

These results are also in agreement with those of Perveen[19] and were also observed by Sterling[33] that increase may be due to super sensitivity of heart to catecholamine in hyperthyroidism and several reports indicate that the number of myocardial β- adrenergic receptors are increased. The information provided by T_4/TBG ratio are valuable, but some discrepancies were observed .On one hand, for every high level of T_4 which is still rising while the T_4/TBG tends to plateau. This situation may result from partial or total saturation of the binding sites of TBG with concomitant elevation of the

free T_4 fraction. When TBG levels are lower and T_4/TBG ratio gives abnormally high values, this is probably results from a major role of other binding proteins like albumin and thyroxine binding pre- albumin when the TBG concentration is decreased or absent. Dumont[21] observed the tissue glucose contents and found increased levels in metabolically highly active tissue and correlated with the degree of hyperplasia of these glands so the higher level of the tissue glucose may be involved in the thyroid pathogenesis.

The correlation coefficient analysis between blood glucose and tissue glucose shows a direct relation (i.e. when glucose concentration in blood increases its concentration will also increased in the tissue) in non toxic goiter patients (r=0.47 P N.S),non toxic nodular goiter (r=0.29) and an inverse relationship was seen in toxic nodular goiter (r= -0.53, p< 0.05) as compared with blood glucose to tissue glucose levels.

Increased glycosylation was found in diabetes mellitus and the increase is directly related to increase in blood glucose level[35]. The results of controls in this study are in agreement with Merelyn[24] and Perveen[19.] Wieland proposed that thyroid hormone enhances the hepatic synthesis of glucose36. The possible mechanism appears to involve induction of the hepatic mitochondrial enzyme pyruvate carboxylase and the cytosolic enzyme phosphoenol pyruvate carboxykinase. These enzymes are responsible for catalyzing the initial reaction of gluconeogenesis form pyruvate. It has also been observed by Elrick et al. that thyroid hormones have a hyperglycaemic effect by two mechanisms[37]. The most important role of T_4 in carbohydrate metabolism is to increase the absorption of glucose from gastrointestinal tract, which increases the gluconeogenesis.

The correlation coefficient of proteins shows an inverse relationship in all the groups(r= -0.38 r= -0.48 and r= -0.87) in non toxic goiter ,non toxic nodular goiter and toxic nodular goiter respectively. But in glycosylated proteins the value of (r) is positive in non toxic goiter and non toxic nodular goiter. Values of(r) in case of protein in toxic nodular goiter is significantly is decreased (r= -0.87). The possible reason may be that thyroid hormone have no effect on the hepatically synthesized protein e.g. albumin, thyroid binding globulin and prealbumin etc but have increased on the endothelium associated protein e.g. fibronectin, F VIII etc. Correlation coefficient of glyosylated proteins show direct proportionality in non toxic goiter and non toxic nodular goiter (r=-0.40, r=-0.13) while (r=-0.12)shows an inverse relation. It was observed that glycosyaltion of protein is particularly important in the maintenance of integrity of plasma membrane and in facilitating the secretion of protein into extracellular space Increased glycosylation was found in diabetes mellitus and ophthalmopathy. The increase is directly related to increase in blood glucose level[24]. The result of controls in this study are in agreement with perveen[19]. Hexosamine has a direct correlation coefficient values of (r =0.23, r=0.14 and r=0.73) in non toxic goiter, non toxic nodular goiter and toxic nodular goiter respectively .Hexosamine contents were estimated to find the variation of aminosugar concentration. Carbohydrate in the thyroiglobulin exist in two type of units. One consisting of only mannose, N-acetyl glucosamine (unit A). The other is madeup of mannose, N-acetyl glucosamie, glactose, fucose and sialic acid residue (unit B)[28,35]. These observation indicate that the concentration of unit A carbohydrate in the non toxic goiter may be more than the toxic goiter groups. Tsuji et al[7] and Yamammoto et al[33] observed that the contents of units A of carbohydrate is decreased with the increase in thyroid hormone because units A appears as an intermediate part.

CONCLUSION

It was concluded from correlation coefficient analysis (blood to tissue levels) that in non toxic goiter and non toxic nodular patients glucose, glycosylated protein and hexosamine showed a direct relationship while protein showed an inverse relationship. In toxic nodular goiter glucose, protein and glycoslated protein show an inverse relationship while hexsoamine has a direct correlation coefficient.

It is suggested research may further be progressed to evaluate the biochemical bases for the conversion of

euthyroid gland into nodular (simple or multi nodular) goiter and even in cancerous form.

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