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RESEARCH ARTICLE

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Correlation between estimated serum Alk-P in newly diagnosed hyperthyroid patients

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ABSTRACT

Thyroid stimulating hormone extensively affects the overall body organ and organ system but mainly it effects on the working of the liver. It has been seen that the drugs indicated for thyroid abnormalities also cause predicaments in liver function. This research work mainly focused on to check the effect of thyroid stimulating hormone abnormality on liver function. The patients were recruited at Center of Nuclear Medicine for routine checkup. The thyroid status of these patients was monitored by finding concentration of triiodothyronine (T3) and thyroxin (T4) that also verified liver function test (LFT). The results appeared with statistical analysis show that there is a strong correlation between disturbed function of thyroid gland and liver function. A variation in thyroid function brings change in liver functioning. Conclusion: During the treatment of thyroid disorder patients, different doses of the medicines to be given for effectively treat the associated disease. The mental status of the patient boosted up by using psychological technique. Furthermore, disease persons which had thyroid dysfunction must be checked the liver function of enzymes. The main causes of the thyroid dysfunction checked from the root if present.

Keyword: Triiodothyronine (T3), Thyroxine (T4), Liver Function Test (LFT), Thyroid Stimulating Hormone (TSH)

1. INTRODUCTION

Thyroid gland is the major endocrine gland which is present in human body. Thyroid gland is found in the neck just below the thyroid cartilage and nearly equal to the cricoids cartilage. Thyroid gland name derived from the Greek word for "shield" after the shape of the related thyroid cartilage. The thyroid controls the energy metabolism of the body, make proteins, and also control the production of the other hormones. Thyroid hormones also play an important role in the development of the brain during the pregnancy [1]. The thyroid gland produce the thyroid hormones in which the

tetraiodothyronine (T4) and triiodothyronine (T3) is 99.9% and 0.1% of thyroid hormones. The most important hormone is T3 which is biologically active and control most of the thyroid gland functions in the body. When the thyroid gland releases its secretions the T4 is converted into the T3 which affects the metabolism of the cells present in body. These hormones control most of the functions in the body in which metabolism and growth are the two important factors. Iodine is an essential component of both T3 and T4. The thyroid gland gets iodine from the different foods like yogurt, eggs, and sea foods. The iodine worked as a stimulator for the proper functioning of TSH.

Hypothalamus is the part of brain which controls the production of thyroid hormones and it is also regulates by almond like shape structure called as the pituitary gland. The hypothalamus which is part of brain produces a hormone called thyrotrophic releasing hormone (TRH), which sends a signal to the pituitary gland that activates the thyroid stimulating hormone (TSH). When the TSH activates it releases the thyroid hormones. After releasing the thyroid hormones the 80% of the T4 is converted to T3 by peripheral organs such as the liver, kidney and spleen and the T3 is nearly about ten times more active than T4. Tetraiodothyronine (T4) is synthesized by the protein of thyroid residue called as the Thyroglobulin (TG) and as well as the by the follicular cells. Iodine is trapped by hydrogen per oxidase which is produces by the enzymes thyroid peroxidase (TPO) and it is link with the 3' and 5' sites of the benzene ring. After the activation of TSH the follicular cells reabsorb TG and break the protein bond of iodinated tyrosine to from TG, then form the T4 and T3 and release them into the blood. Deiodinase enzymes convert T4 to T3. Thyroid hormone that is secreted from the gland is about 90% T4 and about 10% T3. T3 and T4 is the major target of the brain cells. In the blood, T4 and T3 are partially bound to thyroxine-binding globulin, transthyretin and albumin. Thyroid diseases had including the increase or decrease the level of the thyroid gland hormones which causes the overall energy metabolism of the body. The thyroid disorders are commonly affecting the 5 % of the overall population [2].

TSH disease chances are increase with the passage of time. The women had the seven times greater chances of the thyroid diseases as compared to men. The tendency of the thyroid disorder is also depending on the Genetic and as well as the environmental factors. The availability of the too much supply and too low supply of iodine is also effects the functioning of the thyroid gland. The standard quantity of the normal table salt which is prescribed to youngsters is 150ug/day. The chances of the thyroid diseases were also depend on the geographical regions as well as their iodine intake in diet [3].

Hyperthyroidism is a disorder which the TSH releases the excess amount of the triiodothyronine (T3) and tetraiodothyronine (T4). Hyperthyroidism had increased metabolic rate of the body and it had many other symptoms. We suggest many anti thyroid drugs and the surgical treatment used for the hyperthyroidism [4].

Hyperthyroidism is a disorder in which the thyroid gland is overactive and releases the

excessive number of thyroid hormones that circulate in the blood. Term hyperthyroidism and thyrotoxicosis are used interchangeably. Some common causes of hyperthyroidism include: Graves' disease, functioning adenoma ("hot nodule") and toxic multinodular goiter (TMNG), excessive intake of thyroid hormones, abnormal secretion of TSH, thyroiditis (inflammation of the thyroid gland), excessive iodine intake etc. The most common cause of the hyperthyroidism is the over secretion of the thyroid hormone which is further leads to the Graves' disease. In Graves' disease the immune system response abnormally due to this thyroid gland produces too much hormone. This secretion causes the cells had loses its ability to act on pituitary gland via TSH. This disease affects women and men equally. Graves' disease is genetically and auto immune disorder which five times more common among women than men. The triggers for Grave's disease include stress, smoking, radiation to the neck, medications, and infections due to Organisms such as Viruses. An excess production of iodine may cause hyperthyroidism. Iodine-induced hyperthyroidism is mostly seen in those patients who had already over functioning of thyroid gland. Different medications such as amiodarone (Cardamone) which is used in the treatment of heart problems contain a large amount of iodine. These medicines associated with the thyroid dysfunction and cause many other abnormalities like as liver dysfunction.

In hyperthyroid patients many LBT changes had been monitored. These changes which are occurred due to hyperthyroidism patients are due to the use of the anti-thyroid drugs. The drug which is mostly used in the treatment of hyperthyroidism is Propylthiouracil (PTU) it is derived from thioure [5-7]. The use of PTU is not good for the liver it had many side effects and it increases the LBT levels [8-9].

In hyperthyroidism condition some people experience the effect of weight loss while some experience increased appetite and weight gain about 10% of the people due to hyperactive of the thyroid gland. In the female due to the hyperthyroidism the menstrual cycle is also slow, and the menstrual period is also effects due to the hyperthyroidism [10].

Due to the hyperactivity of the thyroid gland every tissue is effected it causes the anxiety, nervousness thinning of skin, hand tremor, heart racing, increased the perspiration, and muscular weakness more effected (upper thighs and arms), sometime the bowl movements of the body is also affected. Hyperthyroidism is varies according to the patient age diet release and excess of hormone secretion and the duration of illness. The older patients and those patients who had older age had some specific type of signs and symptoms which make the measurement of the hyperthyroidism is more difficult [11].

Those patients which had the treatment is continued or not continued they had some time stressful illness or tachycardia, vomiting, fever, dehydration. People which the lymphothyroditis or Graves' disease had given the anti-thyroid drugs which is higher uptake in Graves' disease while the lower up take in the thyroiditis which is useful in treatment. The other parameters which we find from the non-specific laboratory include Anemia, hypercalcemia, agranulocytosis

and higher the levels of the alkaline phosphatases and transaminases.

Pakistan is that country in which the deficiency of iodine is common and mostly the occurrence of the iodine deficiency is most common in northern mountain places [12-13]. Thyroid diseases are mostly common in the coastal areas of Pakistan like as Potwar Plateau, Potwar Balochistan and Salt range [14]. In Pakistan the food consists of less quantity of salt (40 µg/day). This quantity has 3.8 times less than the normal (150 µg/day) used by youngsters [15].

2. METHOD AND MATERIALS

2.1. Research location and participants

One hundred and fifteen (115) patient's sample was collected from different age group 1 to 70 years of male and female at CENUM, Mayo Hospital, Lahore, Pakistan. The recently diagnose patient were passed on to the TSH function test to check the parameter of T3, T4. It was filled questioner to collect the important data about their family history, sign and symptoms. The physical check-up of the neck is done by physical examination. The blood samples of the patient are sent to the laboratory for checking the thyroid parameters FT3, FT4 and TSH.

2.2. Clinical assessment

The previous data about the disease is checked out by the doctor. The previous data included name, age, and gender, use of medication, surgery, neck swelling area and hereditary ancestors. The basic parameters about the thyroid disease were noted. The physical checkup of neck was to determine the present status of thyroid gland size, position and effects to the near body organs.

2.3. Laboratory assessment

The TSH tests performed on the 5ml blood sample. The blood was centrifuge at room temperature by using centrifugation machine for 5 minutes to get antiserum. After centrifuge, the samples were saved at 20°C for future experimentation. The samples were experimented using (RIA) technique and IRMA methodology. The tests were performed by using local available equipment. Serum TPO-Ab test was done into specific patients to check the any autoimmune disorder that attacks the normal tissues.

2.4. Radioimmunoassay (RIA)

The process of Radioimmunoassay, the radio labelled antigen is used. Add the specific amount of the antibody was added in respond to the antigen. The specific quantity of the sample is added to start the reaction. The antibodies release a specific amount of labelled antigen. The amount of labelled and unlabelled antigen was correlated. By using graph, the sample value antigen was determined. This procedure use to determine the values of different hormones or antibodies into the body.

2.5. Sample Material

The enzyme is best measured few hours after withdrawing the blood. The serum or heparin Plasma was separate from the blood.

2.6. Determination of Free Thyroxin (FT4)

T4 have the highest ratio to binding with the protein (99.97%) when T4 binding with the protein it is metabolically inactive. T4 levels were estimated by using different methods like as RIA, ELISA, and EIA. All these methods are specific protein binding. These all assays do not provide specific information about the thyroid disease but the protein binding with T4 must be considered. By using the advance techniques, the free levels of T4 (FT4) have easily determined by checking the metabolically present level of FT4 into the blood. The advance immunoassays techniques to check the concentration of FT4 had ability to calculate the value of FT4 in nanogram quantity of free and biologically active hormone. To calculate the value of FT4 the labeled antibodies are used. The serum test put into the A.C tubes. The T4 monoclonal 125 labeled counter acting agent is additionally included. The response has been continuing between the test of FT4 and biotinylated ligand of T4 about same 125 labeled antibodies. The counter acting agent complexes analog ties with the avidin coated tubes. The amount of radioactive counter acting agent which is ties with the FT4 serum test is contrarily corresponding to the amount of FT4 within the serum test.

2.7. Estimation of the Free Thyroxin

This kit is used to estimate the concentration of the free thyroxin FT4 in blood sample. it was taken a avidin coated tubes. The monoclonal antibody was labeled with I125. The specific glass vial contained 0.00, 2.80, 10.5, 27.6, 76.0 pmol/L of FT4. The tubes were arranged according to the sample number. The sample was added into each tube 25µl.The 400µl amount of the tracer solution was added and checked by 100µl of ligand solution. The tubes were ready that contained the 400µl of tracer (T) to check the (cpm). The tubes were placed on the shaker 350 rpm and incubated at (18-25°C) for 90 minutes. All the tubes were out except of T tubes. Every tube was put on the gamma counter machine for 60sec adjusted the value of I125.

2.8. Immunoradiometric Assay (IRMA)

In this the radio labeled antibody reagent is in large quantity and direct binding had been taken place. Antibody which is bind with the antigen had been calculated and concludes result.

2.9. Estimation of Thyroid Stimulating Hormone (TSH)

In this test the 2nd monoclonal counter acting agent was named with I125 about 1st monoclonal counter acting agent coated tubes. The bounding movement is measured by utilizing gamma counter. TSH concentration is relative to the measured the radioactivity. The undetermined sum of the TSH in tests is checked by the graph.

2.10. Measurement of the Thyroid Stimulating Hormone Concentration

The 100 tubes were coated with monoclonal anti thyroid stimulating hormone antibody. it was required monoclonal i125 and labeled anti TSH antibody. The 200µl of stranded and 100µl of tracer solution was put into sample and agitate gently. The 400µl tracer solution and followed by 100µl of ligand solution. Separate tubes ready that contains the 400µl of tracer (T) solution to check the (cpm). The tubes put on

Table 1. Normal Range of the Heparin in Blood

Gender	Various Temperature		
	25 °C	30 °C	37 °C
Women	40-120 U/L	48-120 U/L	65-240U/L
Men	59-190 U/L	60-220 U/L	80-270U/L
Childs (15 years)	400U/L	480U/L	645U/L
Youngsters (17 years)	300U/L	360U/L	483U/L

Table 2. A.P Normal Values In Growing Age Children

Age 3 to 4 months	730U/L (mean + 2s)
Age 13 to 15 months	702U/L (mean + 2s)

the shaking incubator for 90 minutes at 350 rpm on specific temperature (18-25°C). All the tubes were out except of T tubes. Every tube was put on the G-C machine for 60sec to check the value of I125

3. RESULTS AND DISCUSSION

3.1. Statistical Analysis

In the present study the following statistical parameter were applied to determine the accurate relationship of biomolecule between normal and disease person as means, standard Deviations (SD), standard error of means (SEMs) and P- values. The average value of hypothyroid patients in FT4 is 38.8593. The average value of ALK in hyperthyroid patients is 396.7966. After observing the above values of mean we can interpret that ALK play a significant role in hyperthyroid patients as compared to TSH and FT4. By observing the standard deviation values of hyperthyroid patients (TSH) close to the mean value which means that lower the value of Standard deviation the more concentrated with mean value. Overall, we can say that in hyperthyroid patients the AKLP play a significant role as shown in table 02.

3.2. Comparison Study between Control and Hyperthyroid Patients

Table 3. Study of Statically Parameter on Normal and Disease Sample

Groups		N (Number of Participants)	Mean	Std. Deviation	Std. Error Mean	P-Values
FT4	Control	55	16.9091	2.10205	.28344	
	Hyperthyroid	59	38.8593	13.23540	1.72310	0.00
TSH	Control	55	1.5195	0.69794	0.09411	
	Hyperthyroid	59	.0500	.00000	.00000	0.00
ALK-P	Control	55	220.5091	137.16250	18.49499	
	Hyperthyroid	59	396.7966	186.05235	24.22195	0.04

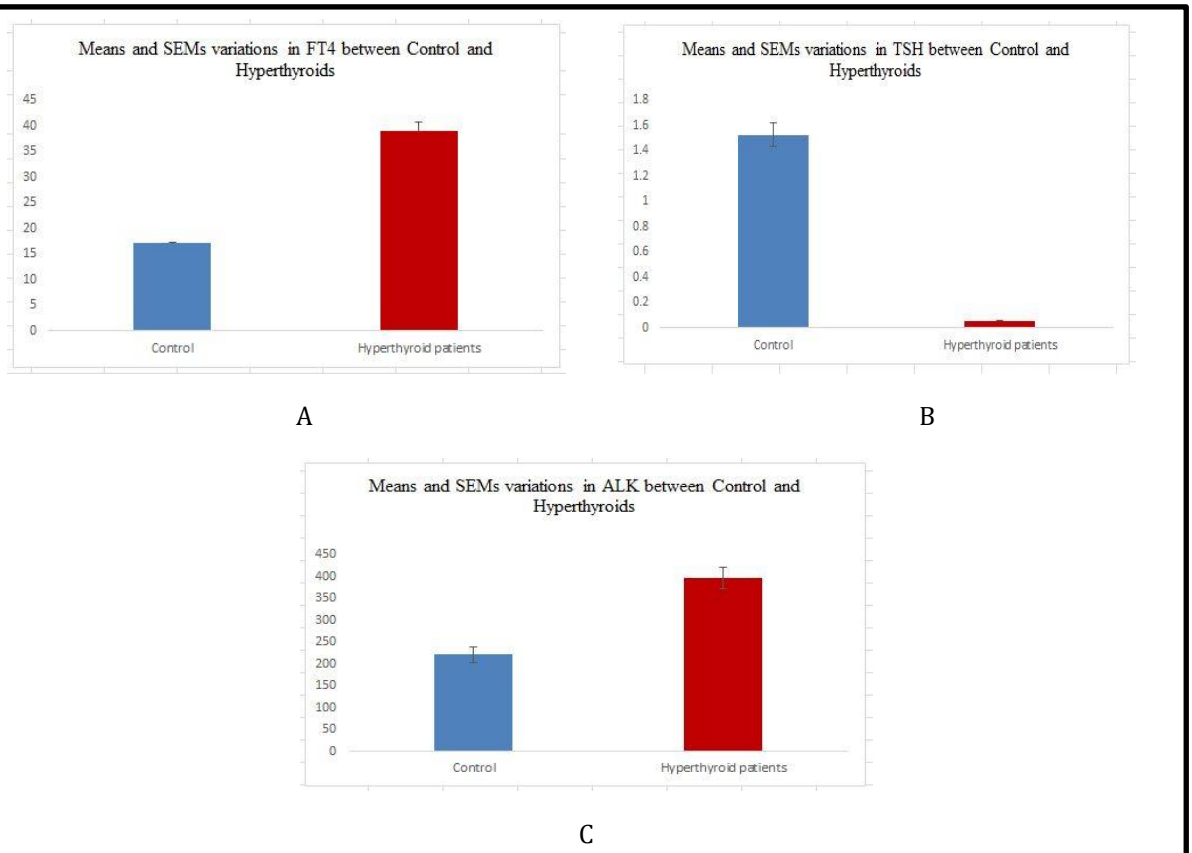

Figure 1. A) Mean and SEM variation in FT4 between Control and hyperthyroid B) Mean and SEM variation in TSH between control and hyperthyroid C) Mean and SEM variation in AL between control and hyperthyroid

The bar chart revealed that the parathyroid concentration in patient is high as compared to control. The fig 01 A) compared FT4 concentration with control. It was also revealed the variation in TSH ALK with control in fig.01B and C respectively. The statistical techniques are applied on the total samples of the control and hyperthyroid population for free tetraiodothyronine (T4) were 16.901, 2.10205 and +0.28344; 38.8593, 13.23540 and+ 1.72310, respectively. These have been shown in figures above and show variations. The values of the hyperthyroid population for thyroid stimulating hormone were 1.5195, 0.69794 and + 0.09411; 0.0500, 0.00000 and + 0.00000 respectively. The standard deviation and standard error of mean were found to be highly changed among controlled and diseased population. The hyperthyroid population for alkaline phosphatase were 220.5091, 137.16250 and + 18.49499; 396.7966, 186.05235 and +24.22195 respectively. Statistical values of this parameter for both study groups i.e., control and diseased, again showed high difference. Significance or non-significance of data was estimated using analysis of variance test among study population for all designed study parameters. P-Values more than 0.01 were set to be non-significant and below 0.01 were considered significant. All study parameters i.e., free tetraiodothyronine (T4), thyroid stimulating hormone and alkaline phosphatase appeared highly significant. The results appeared with statistical analysis show that there is a strong correlation between disturbed function of thyroid gland and liver function. A variation in

thyroid function brings change in liver functioning. The results appeared with statistical analysis show that there is a strong correlation between disturbed function of thyroid gland and liver function. A variation in thyroid function brings change in liver functioning. While treating TSH dysfunction the different doses of the medicines had recommended to effectively resolving the associated disorder. Furthermore, thyroid dysfunction peoples must be checked the LFT's test to find out any abnormality due to any drug side effects.

4. CONCLUSION

The results appeared with statistical analysis show that that every seventh patient of hyperthyroid out of ten has a high level of Alkp. There is also a strong correlation between disturbed function of the thyroid gland and liver function. A variation in thyroid function brings a change in liver functioning. While treating thyroid patients, combination therapy must be recommended to effectively treat the associated disorder and increase the social and psychological status of the patient.

Furthermore, patients coming with thyroid dysfunction must also be examined for liver abnormalities so that the culprit cause of this thyroid abnormality could be treated from the root if present.

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6. CONFLICT OF INTEREST

The authors have declared that there is no conflict of interest.

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NA

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