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Thyroid Function Tests : A Retrospective Study of the Bahraini Population and Establishment of Reference Values

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ABSTRACT

A retrospective study of more than 3000 patients with suspected thyroid illness is reported. These patients were referred to our Radioimmuno Assay Laboratory for thyroid function tests (TFT). The majority of the patients were females. Actual data obtained on the patients suffering from thyroid illness along with data on 500 normal subjects is presented. Results of thyroid function tests carried out on pregnant women are also given. Reference values obtained on normal Bahraini adults for thyroid hormones are also presented.

Measurements of the concentration of thyroid hormones in serum together with assessment of thyroid binding protein are the most commonly employed aids for differentiating between the hypothyroid, euthyroid and thryotoxicosis states. These tests together with a suggestive clinical picture are sufficient to establish an accurate functional diagnosis in the majority of cases [5].

Accurate estimation of Triiodothyronine (T_3), Thyroxine (T_4), Triiodothyronine Uptake and Thyroid Stimulating Hormone (TSH) is now possible with sensitive radioimmuno assay (RIA) method. Free thyroxine index can be calculated from T_3 - uptake and T_4 values.

For suspected thyroid disease, measurement of thyroxine concentration in serum is the first choice investigation in the diagnosis of hypothyroidism or thyrotoxicosis. Serum T_4 levels at birth are higher than values in normal adults, this is due to higher concentration of thyroid binding globulins. T_4 concentration remains constant from the age of five years onwards throughout life.

Suspicion of hyperthyroidism due to higher T_4 values in serum is confirmed by measurements of serum T_3 values. It is also a useful test for following the therapy of hyperthyroid patients and equally useful in avoiding over-treatment in patients with hypothyroidism who are on synthetic T_4 (levothyroxine). In this respect T_3 concentration measurement is more important than T_4 since the concentration of the latter remains high in patients receiving levothyroxine, even though the patients do not appear to be thyrotoxic. At birth T_3 concentration is below normal adult values. It rises continuously and is at peak in approx. 24 hours simulating thyrotoxic level in adults, it then gradually declines during the next few weeks but is still higher (about 25%) than in normal adults through early adolescence [4]. In old age T_3 concentration is lowered due to its decreased peripheral conversion from T_4.

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It is important to assess the hormone binding capacity of serum proteins because it is necessary to ascertain whether a change in total concentration of hormone is due to a change in its binding or change in its production rate. In vitro uptake test, therefore, assumes critical importance in differentiating hypothyroid and hyperthyroid from euthyroid. The product of in vitro uptake value and the serum total T_4 concentration provides so called Free T_4 Index (FTI) which is analogous and varies with Free T_4.

Measurement of TSH concentration is extremely valuable in the diagnosis and management of hypothyroidism, and when used as an index of response to exogenous thyroid releasing hormone (TRH) in the diagnosis of thyrotoxicosis or the differentiation between hypothyroidism of thyroid origin and that due to disease in the pituitary or hypothalamus [3].

The serum TSH concentration is invariably increased in patients with primary hypothyroidism, the magnitude of increase being always proportional to the severity of disease. In cases of mild hypothyroidism where T_4 values may be lower but still in normal range, estimation of TSH helps to confirm the diagnosis when it is found to be elevated. Further, a lower normal TSH level in cases of hypothyroidism excludes primary thyroid failure and suggests dysfunction of the pituitary or hypothalamus.

In the present paper we are submitting a retrospective study of more than 3000 patients referred to our laboratory for thyroid function tests. In addition, we have established a reference range of these parameters for the normal adult Bahraini population.

MATERIAL AND METHOD:

Radioimmuno assay of thyroid hormones was carried out in the serum of patients using reagent kits from Amersham International (UK). The quality of work was checked by using internal as well as external quality control sera. Five hundred adult Bahrainis of both sexes were selected for study to establish reference values for thyroid hormones. Fasting, unhaemolysed and non-lipaemic sera were used for T_3, T_4, T_3-uptake and TSH assays. None of the subjects were suffering from thyroid illness.

RESULTS

A total of 3188 patients were referred to the RIA laboratory for thyroid function tests during the last eighteen months (1983 - 84). The number of male patients were 436 (13.7%) and the remaining 2752 (86.3%) were females. On the basis of laboratory results it was found that out of 436 males 36 were thyrotoxic, 48 hypothyroid and the remaining 352 euthyroid. Out of a total of 2752 females, 165 were thyrotoxic, 203 hypothyroid, 11 T_3-toxic and the remaining 2373 euthyroid. On the basis of TSH results it was found that out of 48 male hypothyroids 39 were primary (Low T_3, Low T_4 and high TSH) and 9 secondary (Low T_3, Low T_4 and normal TSH) hypothyroids. Similarly, out of 203 female hypothyroids 170 were primary and 33 secondary hypothyroids (Table I).

Ninety cases were referred from Ante-natal clinics (30 — 35 weeks of gestation) for thyroid function tests. The majority (82) showed elevated T_4 and normal or slightly elevated T_3 levels but were diagnosed as euthyroid as they showed normalised FTI. The remaining 8 patients were found to be hyperthyroid as elevated T_4, T_3 and increased FTI serum levels were present in these patients. The reference values obtained for serum T_3, T_4, TSH and in vitro T_3-uptake with calculated FTI are shown in Table II. The mean values, standard deviation coefficient of variation and range (Mean $\pm$ 2 SD) for each parameter are tabulated. The mean and SD for serum T_3 were 0.94 and 0.21 ng/ml respectively. The range was 0.52 - 1.36 ng/ml (Mean $\pm$ 2SD) : Mean serum T_4, 7.4 ug/100 ml, SD 1.5 ug/100 ml and range 4.4 — 10.4 ug/100 ml: Mean serum T_3 — uptake 29%, SD 1.4% and range 26.2 — 31.8 : Mean FTI 2.2, SD 0.4 and range 1.4-3.0 ug/100 ml. TSH mean 2.1, SD 1.4 and range 0-5 uU/ml. The coefficient of variation (CV) for each parameter is also calculated and tabulated.

Figures 1 — IV show graphic distribution of T_3, T_4, T_3 - uptake and FTI values actually obtained in normal subjects (euthyroid), hypothyroids and thyrotoxic patients. TFT values obtained in Antenatal clinic patients are also given. Each dot represents an actual data point.

DISCUSSION

It is a well known fact that thyroid illness predominantly affects females. 86% of cases referred to our laboratory for thyroid function tests were females, 13% of females referred were found to be suffering from thyroid illness (6% hyperthyroids and 7% hypothyroids). 78% female hypothyroids were primary and the remainder secondary hypothyroids. In

TABLE - 1

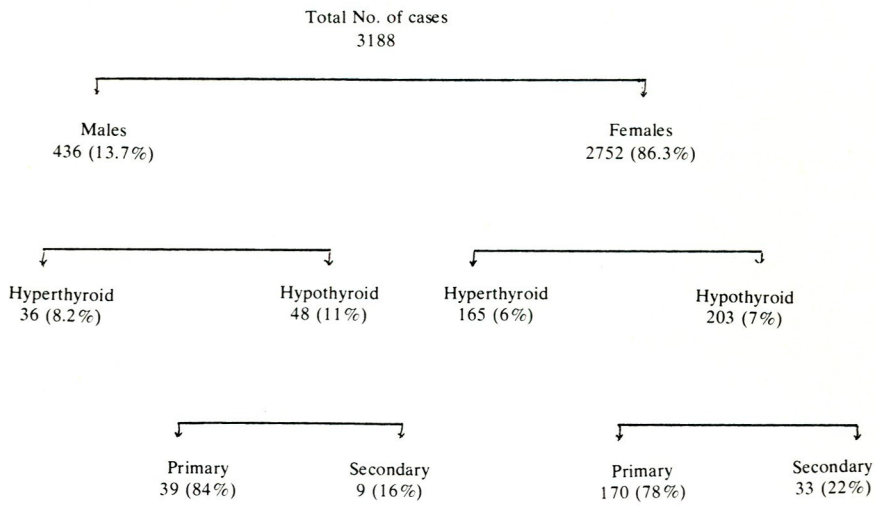

Table I
Incidence of thyroid disease amongst the no. of patients referred to RIA lab. for thyroid function tests.

TABLE - II

	T_3 ng/ml	T_4 ug/100 ml	T_3 uptake percent	FTI ug/100 ml	TSH uU/ml
Mean	0.94	7.4	29	2.2	2.1
S.D	0.21	1.5	1.4	0.4	2.8
C.V	22 %	20%	4.8%	18%	-
Range	0.52 - 1.36	4.4 -10.4	26.2-31.8	14-30	0 - 5

Table II : Reference values (Mean $\pm$ 2 SD) obtained for T_3, T_4, T_3-uptake, FTI and TSH in the blood of normal Bahraini adults (n = 500).

FIGURE I

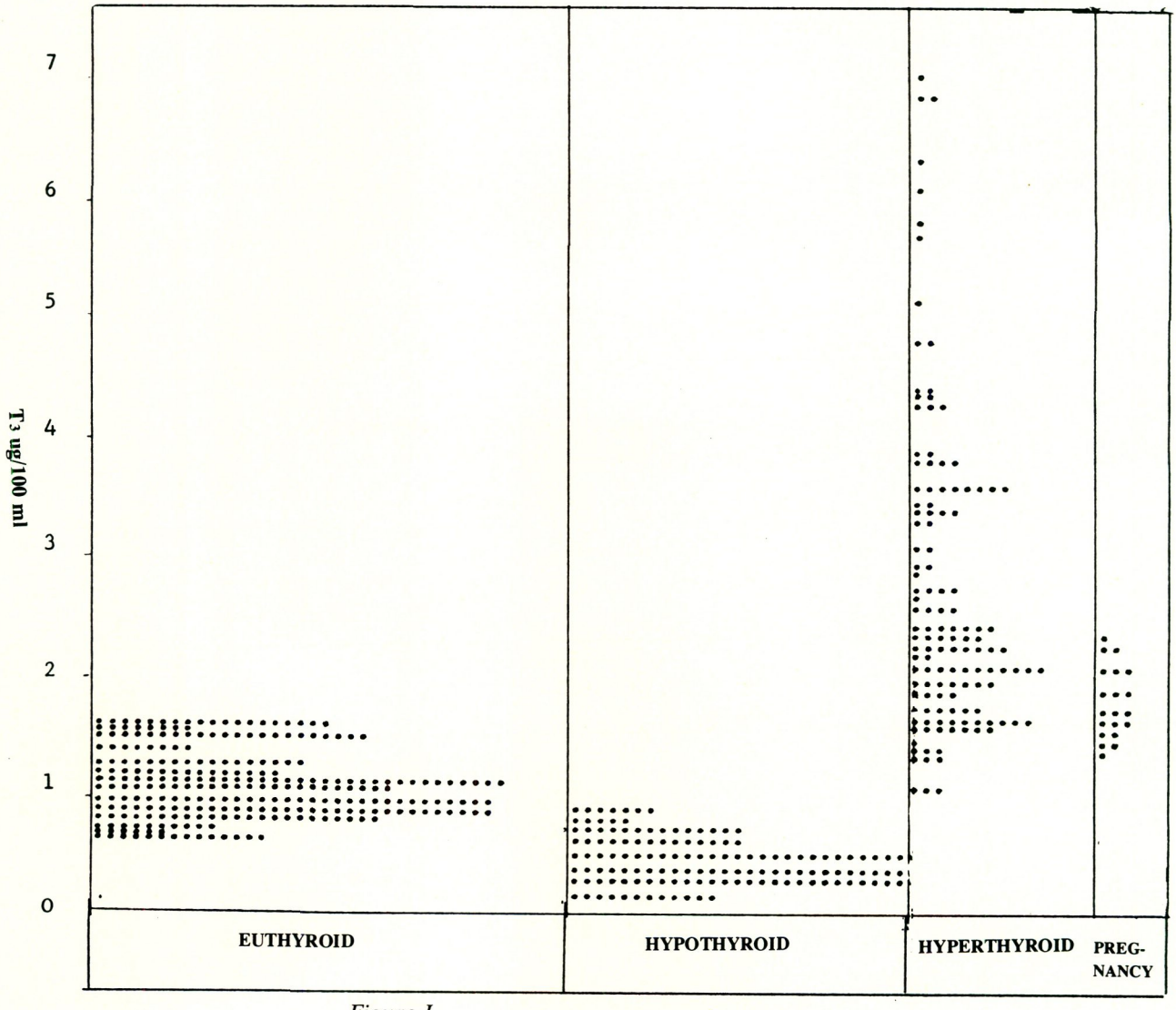

Figure I
Distribution of serum T3 concentration in euthyroid, hypothyroid, hyperthyroid and pregnant patients. Each dot represents actual data point.

FIGURE II

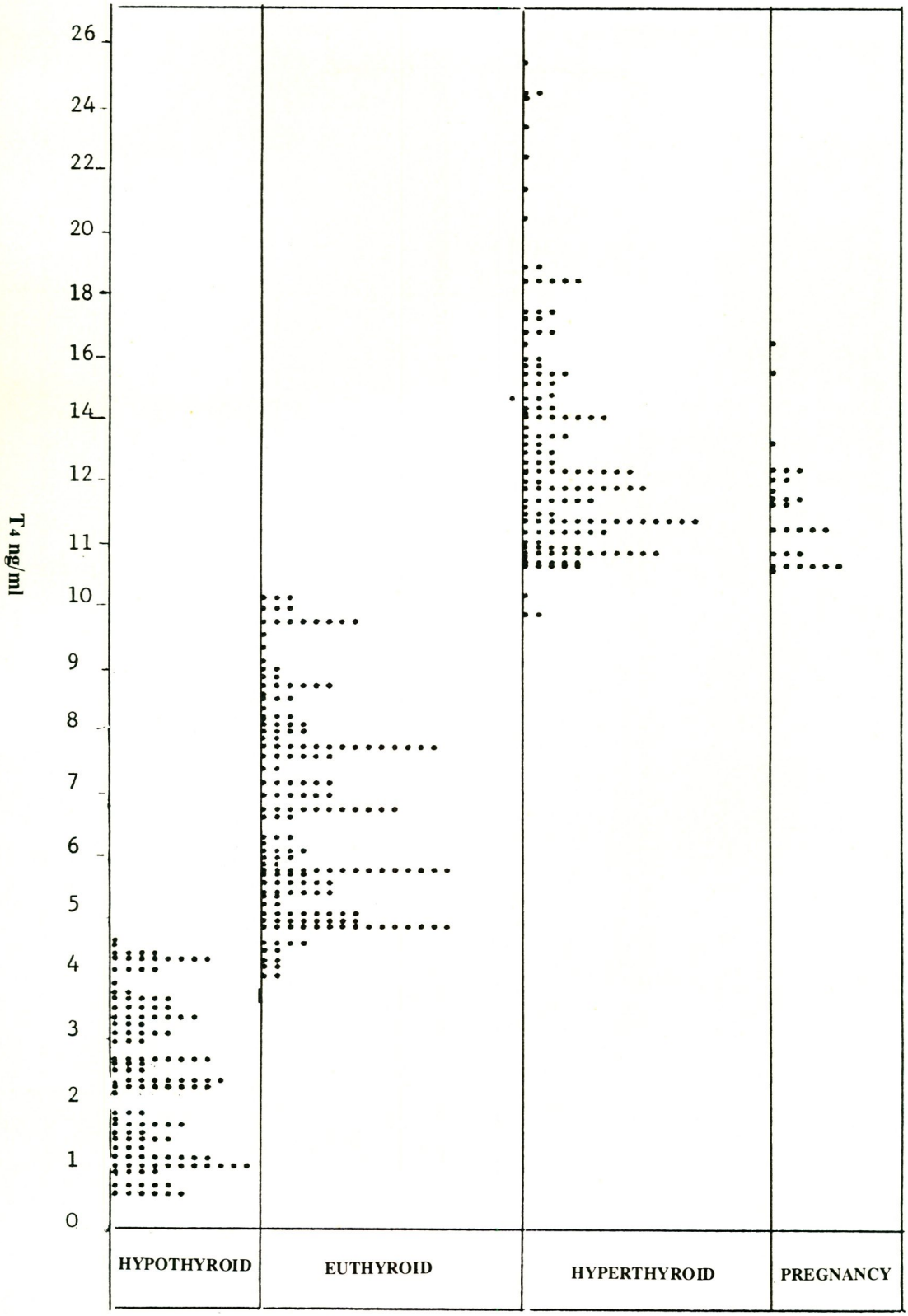

Figure II
Distribution of serum T4 concentration in euthyroid, hypothyroid, hyperthyroid and pregnant patients. Each point represents actual data point.

FIGURE III

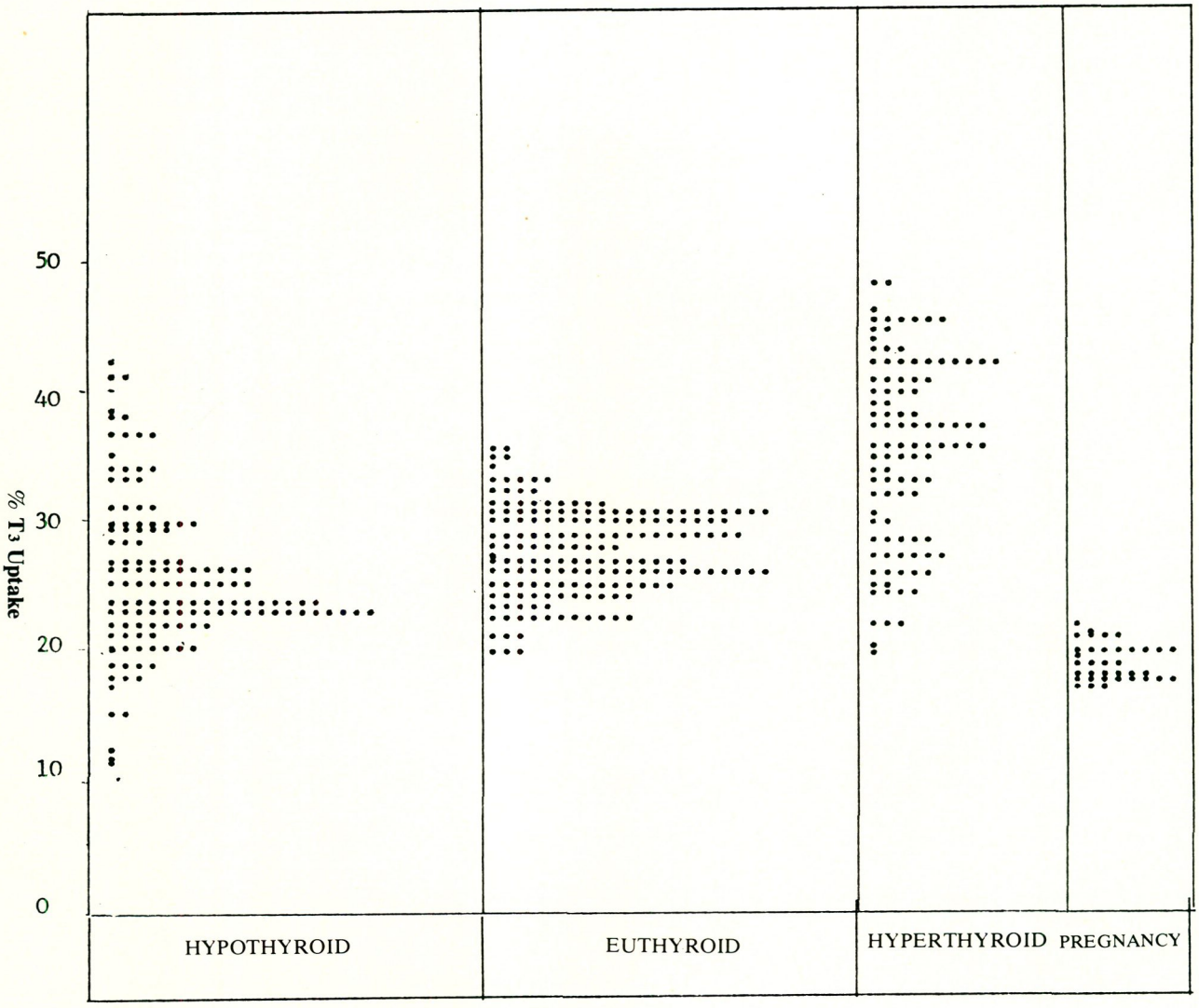

Figure III
Distribution of vitro T_3 uptake values in euthyroid, hypothyroid, hyperthyroid and pregnant patient. Each dot represents actual data point.

FIGURE IV

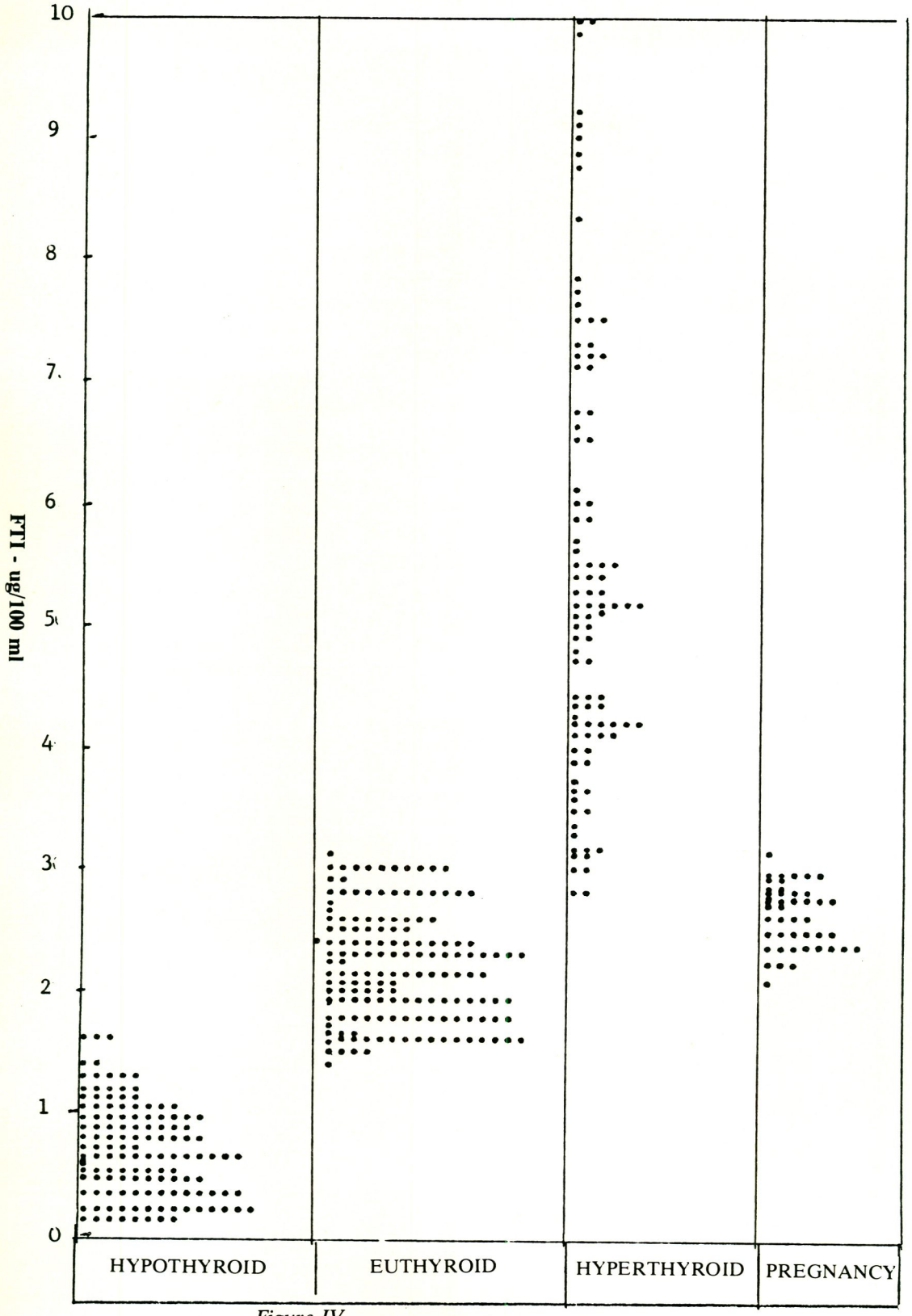

Figure IV
Distribution of serum Free Thyroxine Indices in hyperthyroid, hypothyroid, euthyroid and pregnant patients. Each dot represents an actual data point.

males we found 8.2% cases of hyperthyroid and 11% cases of hypothyroids, the majority being primary (84%). Eleven cases of T_3-toxicity were detected, all cases were females and had high T_3 and normal T_4 serum values. It is important to correct T_4 values specially when both T_4 and T_4 binding proteins are changed for physiological reasons not associated with thyroid disease. A common example of this is when circulating oestrogen levels are high, such as in pregnancy or during administration of oral contraceptives. In these cases circulating T_4 levels are high and on this basis a false diagnosis of hyperthyroidism might be made. However, the levels of binding proteins are also elevated and thyroid hormone binding capacity is increased [1]. The combination of T_4 values and a T_3 uptake value gives FTI values that place the subject in the euthyroid range of the FTI scale. In the present study we found that the majority in Antenatal clinic cases referred to us for thyroid function tests had FTI in the euthyroid range.

Figures 1 — IV illustrate clearly the distribution of TFT values in euthyroids hypo and hyperthyroids as well as in pregnancy. Except for a few borderline cases, TFT are valuable diagnostic tests reflecting the thyroid status of a patient. Normal TSH values in patients having T_4 values at the lower end of reference range rules out hypothyroidism. Similarly TSH estimation is valuable in differentiating between primary and secondary hypothyroids. In some cases it would be necessary to carry out thyroid releasing hormone induced TSH estimation to establish integrity of hypothalamus — pituitary — thyroid axis.

The reference range obtained for T_3, T_4, TSH, T_3-uptake and FTI are shown in Table II. The range for these parameters are not significantly different from those established by other laboratories using the same reagent kits [2]. There is no significant difference between males and females for these parameters. All the subjects were in the age group of 18 - 50 years.

CONCLUSION

This study involving 3000 patients who are citizens of Bahrain brings to light the fact that the incidence of hypothyroidism and thyrotoxicosis is 7% and 6% respectively in females and 8% and 11% in males. Further, the reference values for Thyroid Function Tests conform to the values obtained by others using the same technique and reagents.

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be better to gradually correct hyponatraemia and volume contraction by infusion of normal saline rather than using hypertonic NaCl solution [4 6 15]. Management of the acid-base disturbances followed the same lines. Volume expansion with saline and correction of hypokalaemia were accomplished by gradually normalising Pa Co2 in order not to have major PH drifts if one disturbance is corrected faster than the other[8 10]. The patient also received sodium acid phosphate 45 meq daily for a few days.

As it was mentioned earlier, after a few days of intensive therapy which resulted in significant correction of the problems, the patient was weaned from the ventilator according to the usual criteria [2 12].

This demonstration is further proof that the successful saving of patients lives can be achieved by intensive combined team work.

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