# HAEMATOLOGICAL CHANGES IN THYROTOXIC PATIENTS IN SINGAPORE

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## SYNOPSIS

**The records of 152 thyrotoxic patients (30 males, 122 females) diagnosed and treated in Medical Unit One, Singapore General Hospital between January 1979 and August 1980 were reviewed. 11% of the patients had a nonspecific anemia and 70% had a tendency towards microcytosis at the diagnosis of thyrotoxicosis. Both abnormalities were reversed when the patients achieved euthyroid state. No megaloblastic anemia was encountered. The frequencies of $\alpha$ and $\beta$ thalassemia minor were respectively 2.2% and 3.6% which were comparable to those of the normal Singapore population. Abnormal hematological concomittants of thyrotoxicosis appear to be restricted to minor reversible red cell changes namely, an uncomplicated, mild anemia and the tendency towards microcytosis.**

## INTRODUCTION

Much has been written concerning haematological aberrations in myxedema. Surprisingly little, however, is known about haematological changes in thyrotoxicosis. Until four years ago it was generally accepted that there were no characteristic haematological concomittants of hyperthyroidism. Then in 1976, quite by accident, Horton et al observed, while studying the haematology of myxedema, that microcytosis without iron deficiency was common in thyrotoxicosis (1). This observation was confirmed two years later by Nightingale et al who also reported increased incidences of pernicious anemia (1.9%) and nonspecific anemia (28% in men and 18% in women) among their hyperthyroid patients (2). Intrigued by these observations made on Caucasian patients we conducted a similar study and we report here the findings in our local thyrotoxic patients.

## METHOD AND RESULTS

Our study was conducted on patients diagnosed and treated in the University Department of Medicine, Medical Unit One, Singapore General Hospital between January 1979 and August 1980. To be included patients had to have the following criteria (1) be clinically thyrotoxic (2) had biochemical confirmation of hyperthyroidism and (3) had a full blood cell count (by the Coulter S counter), platelet count and ESR before the commencement of antithyroid therapy.

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Over this twenty month interval, a total of 152 thyrotoxic patients were registered in the unit. Of these 122 were females and 30 males, giving a female to male ratio of 4:1. Patients were predominantly Chinese, making up more than 95% of the total (Table 1).

**THYROTOXICOSIS : TABLE 1**
**SEX/RACIAL DISTRIBUTION**

| SEX | CHINESE | NON-CHINESE | TOTAL |
|---|---|---|---|
| MALES | 27 | 3 | 30 |
| FEMALES | 118 | 4 | 122 |
| TOTAL | 145 | 7 | 152 |

Majority were in their third or fourth decade of life with few in either extremes (Fig. 1). The oldest patient was a 79 year old man and the youngest an 11 year old girl.

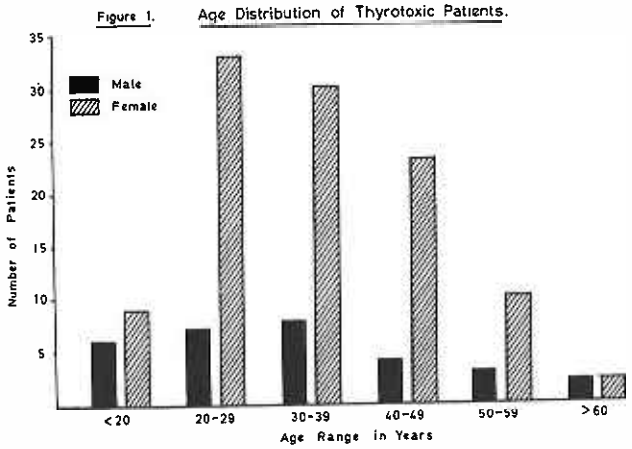


Figure 1: Age distribution of thyrotoxic patients.

Of the 152 patients, 15 (all females) were excluded from the study because full blood cell counts were not recorded at the time of diagnosis. The remaining 137 patients had full counts documented at the outset. Of this group 4 males and 17 females were found to have haemoglobins of less than 13 gm% and 12 gm% respectively (Table 2). Thus according to the World Health Organisation haemoglobin criteria (13 gm% for men and 12 gm% for women), 21 out of the total of 137 patients had anemia at the diagnosis of thyrotoxicosis.

Investigations into the underlying causes for anemia revealed 3 cases of iron deficiency, 3 cases of Thalassemia minor, no megaloblastic anemia and 15 cases of nonspecific anemia (Table 3). The overall prevalence of nonspecific anemia in our group of thyrotoxic patients was 10.9% (Table 4).

**THYROTOXICOSIS : TABLE 2**
**ANEMIA IN THYROTOXIC PATIENTS**

MALE Hb 13 GM %
FEMALE Hb 12 GM %

| SEX | TOTAL | ANEMIA |
|---|---|---|
| MALES | 30 | 4 |
| FEMALES | 107 | 17 |
| TOTAL | 137 | 21 |

**THYROTOXICOSIS : TABLE 4**
**PREVALENCE OF NONSPECIFIC ANEMIA**

| SEX | TOTAL | NONSPECIFIC ANEMIA | % |
|---|---|---|---|
| MALE | 30 | 3 | 10 |
| FEMALE | 107 | 12 | 11 |
| TOTAL | 137 | 15 | 10.9 |

22 males and 85 females had mean corpuscular volumes (MCV) of less than 85 fentolitres (cubic microns) at the diagnosis of thyrotoxicosis, 85 fentolitres being the mean for the local MCV. Causes for diminished MCV revealed 3 cases of iron deficiency and 8 cases of thalassemia minor. Ninety-six patients had undefined reduced MCV giving a prevalence of 70% (Table 5) unexplained low MCV.

There were a total of 8 cases of Thalassemia minor of which 3 were alpha minor and 5 beta minor (Table 6). This gave a prevalence of 2.2% and 3.6% respectively of alpha and beta minor thalassemia. These figures are similar to those observed for the normal Singapore population.

On achieving euthyroid state, as determined clinically and biochemically, a full blood cell count was repeated on all previously anemic patients and those who had reduced MCV at the time of diagnosis of thyrotoxicosis. All 15 patients (3 males and 12 females) who had a nonspecific anemia at the outset showed a rise in haemoglobin without specific therapy apart from their antithyroid drugs (Fig. 2). The average rise in haemoglobin was 1.8 gm%. This is an interesting observation as it suggests that a mild, uncomplicated anemia can be a concomittant finding in thyrotoxicosis which can be reversed by merely treating the hyperthyroid state.

Of the 85 females with reduced MCV at diagnosis, follow up full blood cell counts were available on 47 patients. Of the 38 patients not followed, 16 were still clinically thyrotoxic in August 1980 and 22 failed to return when called to report for full blood counts. The mean corpuscular volumes of the 47 female patients at diagnosis and following achievement of euthyroid state are shown in Figure 3. The average rise in MCV

**THYROTOXICOSIS : TABLE 3**
**TYPES OF ANEMIA IN THYROTOXIC PATIENTS**

| SEX | TOTAL | IRON DEFICIENCY | MEGALOBLASTIC ANEMIA | THALASSEMIA MINOR | NONSPECIFIC ANEMIA |
|---|---|---|---|---|---|
| MALES | 4 | — | — | 1 | 3 |
| FEMALES | 17 | 3 | — | 2 | 12 |

**THYROTOXICOSIS : TABLE 5**
**CAUSES OF REDUCED MEAN CORPUSCULAR VOLUME**

| SEX | TOTAL | M C V <85 fl | IRON DEFICIENCY | THALASSEMIA MINOR | UNDEFINED LOW MCV | % |
|---|---|---|---|---|---|---|
| MALES | 30 | 22 | — | 2 | 20 | 66 |
| FEMALES | 107 | 85 | 3 | 6 | 76 | 71 |
| TOTAL | 137 | 107 | 3 | 8 | 96 | 70 |

**THYROTOXICOSIS : TABLE 6**
**INCIDENCE OF THALASSEMIA MINOR**

| SEX | THALASSEMIA MINOR (α) | THALASSEMIA MINOR (β) |
|---|---|---|
| MALES | — | 2 |
| FEMALES | 3 | 3 |
| TOTAL | 3 | 5 |
| % | 2.2 | 3.6 |

Figure 2

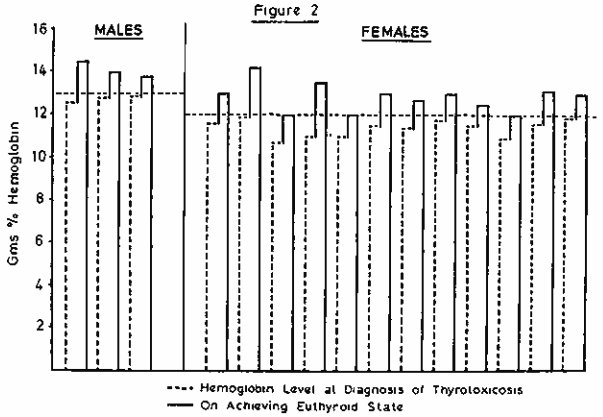


Figure 2: Improvement of haemoglobin level on achievement of euthyroid state.

following euthyroid state was 5 cubic microns. Similarly the male follow-ups showed a comparable rise in MCV following therapy with antithyroid drugs (Fig. 4).

The other haematological parameters looked at in our study were platelet count, total white cell count and erythrocyte sedimentation rate (ESR). No deviation from the normal was observed for the group as a whole on these parameters. Where deviation from the normal was noted in any given patient, an obvious secondary cause was invariably present.

## DISCUSSION

Why does thyrotoxicosis produce a mild anemia or an increased tendency towards microcytosis? We know that in myxedema the anemia is related to reduced metabolic rate and hence the need for tissue oxygen. In thyrotoxicosis, on the other hand, there is increased metabolic rate and increased tissue oxygen consumption. Anemia, therefore would appear inappropriate in thyrotoxicosis. However, we also know that in thyrotoxicosis the various intracellular metabolic processes are accelerated. Specific to the red blood cells, it is known that the level of 2, 3 diphosphoglyceraldehyde

Figure 3

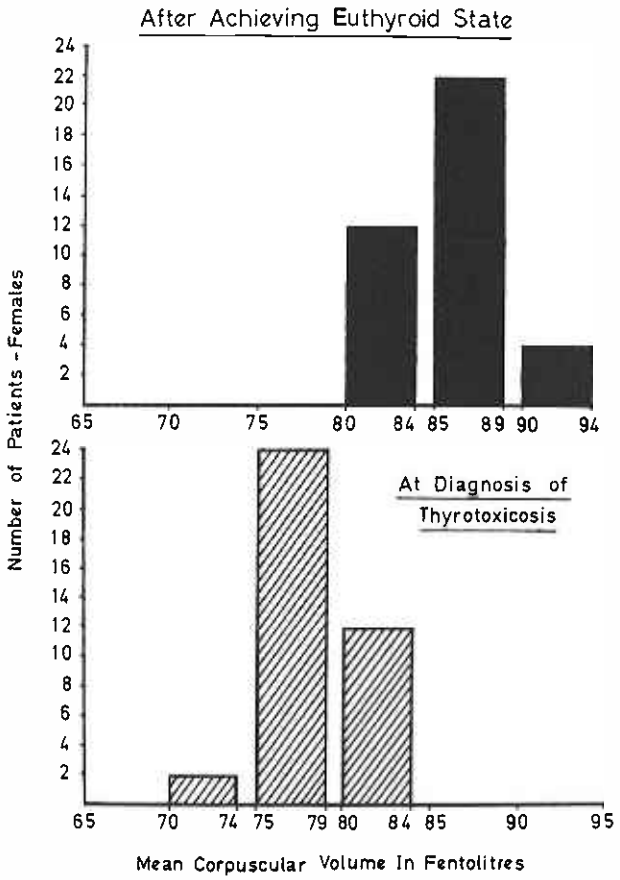


Figure 3: Mean corpuscular volumes at diagnosis and on achieving euthyroid state in female patients.

(2, 3-DPG) is increased in thyrotoxicosis. This shifts the oxygen dissociation curve to the right, making oxygen more readily available to the tissue cells. This increased availability of oxygen from the haemoglobin molecule may be the reason behind the mild anemia observed in hyperthyroid patients. The ultimate proof for this postulate lies in the demonstration that P50 (the partial pressure of oxygen when the haemoglobin saturation is 50%) is raised (greater than 37 mm Hg) in those patients with a nonspecific anemia at the diagnosis of hyperthyroidism. Unfortunately we do not have the facility for measuring P50.

The tendency towards microcytosis is a feature classically of iron deficiency and the thalassemias. In our study these causes account for only 11 of the patients. Microcytosis may also be a feature of long standing chronic inflammatory conditions where ineffective iron re-utilization leads to anemia and red cell changes. Apart from their thyrotoxic state, our

Figure 4

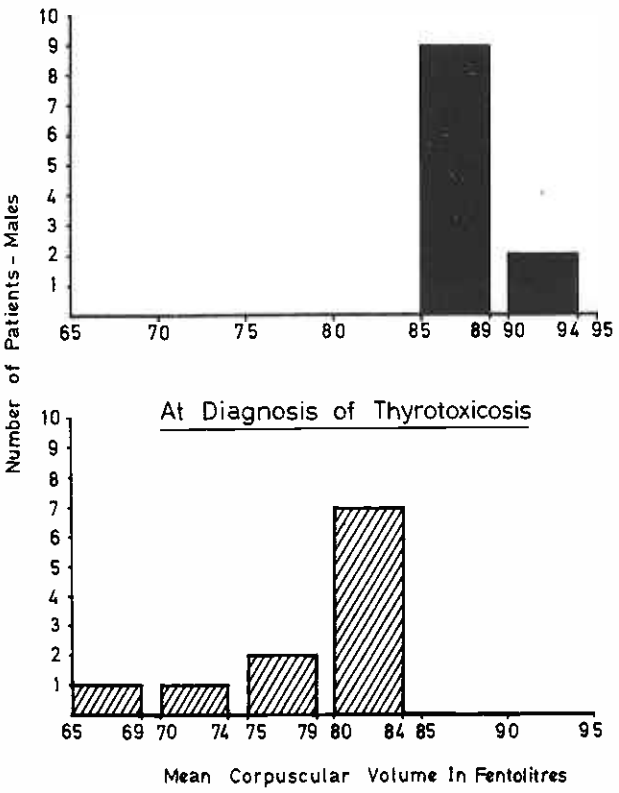


Figure 4: Mean corpuscular volumes at diagnosis and on achieving euthyroid state in male patients.

patients with diminished MCV had no associated chronic medical disorders. As 70% rather than 100% of the patients showed this tendency towards microcytosis at the outset, could the duration of the hyperthyroid state prior to diagnosis influence red cell development? We were unable to substantiate such a relationship as the duration of symptoms frequently was not documented. An alternate explanation, although a teleological one, for the diminished MCV is that it is probably an adaptation to meet the increased tissue oxygen demand in the thyrotoxic state. Smaller cells provide a relatively larger surface area per cell whereby oxygen diffusion into the cell and hence haemoglobin oxygenation are facilitated. Thus the oxygen carrying capacity per red cell should be improved. Nightingale et al (2) suggested that increased erythropoiesis in the hyperthyroid state is responsible for the formation of smaller red cells such as is seen in the thalassemias. This analogy does not hold for the microcytosis seen in iron deficiency anemia where it is well known that erythropoiesis is depressed when iron is depleted. There are at present no satisfactory explanations to account for the minor red cell changes observed in thyrotoxic patients.

## CONCLUSIONS

From our study the following observations can be made:

(1) We found no significant changes in the platelet and total white cell count in our patients.

(2) Megaloblastic anemia was not encountered in the study.

(3) Despite the tendency towards microcytosis we observed no increased incidence of Thalassemia minor.

(4) The haematological concomittants of thyrotoxicosis in Singapore patients appear to be limited to minor red cell changes which include (a) a mild, nonspecific anemia and (b) a tendency towards microcytosis, both changes being reversible on achieving the euthyroid state.

## REFERENCES

1. Horton L, Coburn RJ, England JM and Himsworth RL: The haematology of hypothyroidism. Q J Medicine 1976; 45: 101-124.
2. Nightingale S, Vitek PJ and Himsworth RL: The haematology of hyperthyroidism. Q J Medicine 1978; 47: 35-47.