The E. V. Pieris Memorial Oration

Iodine excretion, goitre and thyroid autoimmunity in Sri Lanka — the current status and lessons for the future

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Background

Iodine deficiency and endemic goitre are found in large areas of the world spanning almost all the continents. Data from the UNICEF from 1995 reveals a population at risk of 1.6 billion of whom 555 million have visible or palpable goitre. Brain damage is estimated to be present in 26 million and cretinism in 5.7 million. Although goitre is thought to be a recent disease in Sri Lanka, there is a large body of evidence to suggest that there is a high prevalence of goitre (specially amongst women) with the highest rates being found in the wet zone (compared to the dry zone). Iodine levels in food, water and soil were reported to be low from the same areas. The most recent survey reported prevalence rates of up to 30% in some parts of the country.

Iodine metabolism in humans

The thyroid gland concentrates iodine obtained mainly from dietary sources, under the influence of TSH secreted by the pituitary gland. TSH is both a secretagogue and a trophic hormone. The free T4 and free T3 so produced are involved in a neat feed back mechanism, which fine-tunes the whole system. Almost 90% of ingested iodine (current recommendations by the ICCIDD/WHO for non-pregnant individuals being 150-200 mcg/day) is excreted in the urine (>100 mcg/l). The components of this system lend themselves ideally to the monitoring of iodine economy in humans. Thyroid volume (measured by ultrasound techniques), urine iodine excretion (measured in spot samples) and TSH levels (particularly in neonates) are the current ICCIDD recommended indices for studies of iodine status and goitre prevalence in communities.

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The 1998 study

Aims

We aimed to study three groups of vulnerable individuals (schoolchildren, pregnant females and neonates) in areas of the country previously shown to have low, intermediate and high goitre prevalence.

Methods

Schoolchildren and pregnant and non pregnant women

We visited randomly selected schools in Colombo, Kandy, Matale, Kalutara and Galle after obtaining consent from the education authorities and parents. Pregnant and non-pregnant control women were seen at the academic unit of the Galle Maternity Hospital. Thyroid volumes were measured using previously validated ultrasound scan techniques. Spot samples of urine and blood samples were obtained from each schoolchild, and pregnant and control woman for assessing urine iodine excretion, TSH, free T3, free T4, antithyroid peroxidase (TPOAb) and antithyroglobulin (TgAb) antibodies. Anthropometric data were also collected using standard validated methods.

Neonates

Neonates were visited at 4-5 days after birth and heel prick blood spots were obtained for TSH estimation.

Results

Schoolchildren

Data from 367 schoolgirls between the ages of 11-16 years, were available for analysis.

Thyroid volume (TV)

Age	11	12	13	14	15	16
TV (mls) Mean	5.1±1.5	6.7±2.1	6.8±2.2	6.8±3.6	8.4±3.4	8.9±3.1
Median	4.8	6.2	6.1	7.7	7.7	8.6
WHO/ ICCIDD Median	5.7	6.3	7	7.7	8.4	
P^{97}	9	10.4	12	13.9		

There was no significant thyroid enlargement compared to WHO/ICCIDD data from iodine replete areas. There was an expected age related increase in thyroid volume. Goitre prevalence was less than 4%.

Median thyroid volumes expressed in relation to age and body surface area were not significantly different compared to a European reference population and was well below the 97th percentile.

Urinary iodine excretion

Age	11	12	13	14	15	16
UI (mcg/L) Mean	158±65	168±81	151±85	145±67	149±94	145±82
Median	134	152	126	125	105	134

Median iodine excretion was normal compared to iodine replete areas in all age groups.

Thyroid function

Thyroid function was normal in 363 subjects. TSH was raised in 4 subjects (5.03-41.29 mU/l) with normal free T4 and free T3. There was no evidence of iodine induced thyrotoxicosis.

Antithyroid antibodies

There was a high age related prevalence of TgAb in the schoolgirls studied (range 11-69%). The prevalence of TPOAb remained < 10%.

Pregnant women

Eighty-four pregnant women from the three trimesters and an equal number of age and parity matched non pregnant women were analysed.

Thyroid volume

There was a 20% increase in median thyroid volumes in the third trimester over non-pregnant values.

Urine iodine excretion

Urine iodine excretion was normal in the non-pregnant controls and increased during the three trimesters of pregnancy.

Neonates

Heel prick blood samples have been obtained from 612 neonates on the 4-5th day after birth. TSH levels have been under 10 mU/l in all subjects.

Conclusions

The current position compared to WHO/ICCIDD standards is as follows -

Variable	Normal WHO/ICCIDD	Mild IDD	Severe IDD	Sri Lanka
Prevalence of goitre in SAC %	< 5	5-19.9	> 30	≤ 4
(%) of TV > P^{97} by US scan	< 5	5-19.9	> 30	≤ 4
Median UI	100-200	50-99	< 20	105-152
(%) of Neonatal TSH > 10	< 3	3-19.9	> 40	Nil

The present study confirms that there is no significant thyroid enlargement amongst 11-16 year old schoolgirls in the population sampled. Goitre rates were < 4%. Iodine excretion rates reflected an adequate iodine intake. However, the increased age related prevalence of TgAb, is an unusual feature and has not been reported before in a population based study.

Thyroglobulin is an iodinated molecule and there is ample evidence to suggest that iodinated Tg is more immunogenic than poorly iodinated Tg. Salt iodination is a legal requirement in Sri Lanka. However, there is recent evidence to suggest that only about one third of randomly selected samples of cooking salt were iodinated to recommended levels. More than half were iodinated to above and 16% to below these levels. This raises serious concerns about the deleterious effects of over iodination as the high prevalence of TgAb may reflect an exuberant immune response to over iodinated Tg molecules. The long-term prognostic significance of a high prevalence of TgAb is speculative and the significance of TgAb in the pathogenesis of autoimmune thyroid disease is not clear. There is evidence for both a pathogenic role (when epitope expression on the Tg molecule is restricted) and for TgAb production as an epiphenomenon. On going studies undertaken by us with monoclonal antibodies raised against epitopes on the Tg molecule would help elucidate this issue.

Recommendations

Urgent priorities for Sri Lanka

Monitoring adequacy and unwanted effects of iodination

Larger studies of a similar nature are needed from different geographical locations in the country for strengthening the findings of the current study. Iodine induced thyrotoxicosis, previously reported from Tasmania, Zaire and Zimbabwe, needs to be guarded against. The high prevalence of TgAb is a cause for concern in this respect as it may herald the onset of overt autoimmune thyroid disease.

Establishing a central monitoring committee with laboratory facilities

There is an urgent need to set up a central statutory body for the purposes of monitoring iodination of salt. A high quality laboratory for biochemical monitoring of thyroid function, thyroid autoimmunity, and urine iodine excretion should be set up urgently. This laboratory may indeed be a regional laboratory (given the expertise in Sri Lanka) serving Sri Lanka and its neighbours. Such a laboratory has been set up in China recently.

Study of other factors responsible for goitre formation

Recent evidence that selenium deficiency exists in areas with a previous high prevalence of goitre needs to be pursued. A comprehensive study of dietary and nutritional factors should be undertaken.

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