Afr J Med med Sci (1998) 27, 57-61

Maternal and neonatal thyroid status in Saki, Nigeria

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Summary
The influence of inadequate iodine intake on maternal and neonatal thyroid status in Saki, a locality known to have environmental iodine deficiency and located within the goitre belt of Southwestern Nigeria was investigated. One hundred and five (105) subjects and ninety (90) controls from Ibadan were recruited into the study. All subjects were apparently healthy with at least thirty-seven (37) completed weeks of gestation. Each subject was assessed for goitre and blood sample obtained by venepuncture for thyroid function tests before onset of labour. Spot urine samples were also obtained from the mothers at the time of examination for urinary iodine estimation. At delivery, cord blood samples were obtained from the babies for thyroid function tests. The mean maternal urinary iodine excretion was significantly less in Saki when compared with Ibadan (144.76 ± 14.68 vs 213.36 ± 9.89 ug/L $P < 0.01$). Maternal total goitre rates (TGR) were 46.8% and 2.2%, while maternal visible goitre rates (VGR) were 26.6% and 1.1% in Saki and Ibadan, respectively. Maternal mean plasma total T3 and total T4 were relatively lower in Saki as compared to Ibadan, though the differences were not statistically significant. Mean maternal plasma TSH in Saki was slightly above our laboratory reference interval (0.3 – 5.0 mU/L) and higher than the level seen in Ibadan mothers (6.54 ± 1.58 vs 4.18 ± 1.37 mU/L,), though the difference was also not statistically significant. Mean neonatal total T3 and T4 were lower in Saki when compared to Ibadan, but the differences were not statistically significant. The mean neonatal plasma TSH in Saki was above the adult reference interval and significantly higher than the level seen in Ibadan (9.82 ± 1.64 vs 4.18 ± 1.17 mU/L, $P < 0.05$). The incidence of neonatal chemical hypothyroidism (NCH) in Saki was 14.7 per 1000 babies. No case of NCH was seen in Ibadan. These results suggest environmental iodine deficiency and relative chemical hypothyroidism of mothers and neonates in Saki when compared to mothers and noenates from non-iodine deficient areas.

Key-words: *Iodine deficiency, endemic Goitre, hypothyroidism, cretinism*

Résumé
L'effet de l'influence de la consomation inadequate de l'iode sur le status de la tyroide maternelle et neonatale a été investiguer à Saki, une localite reconnut avoir une deficience en Iode environmental, et situé dans la ceinture de goitre du sud-ouest du Nigeria. Cent-cinq (105) sujets et 90 controles d'Ibadan avait été recrutés pour l'étude. Tous les sujets étaient apparement en bonne sante et avaient au moins 37 semaines complète de gestation. Chaque sujet avait été examiné pour le goitre et les specimens sanguins obtenue par la veine pour les testes de la tyroide avant le debut de l'étude. Les specimens urinaires avaient aussi été obtenuent des mères au moment de l'examen pour estimer le taux d'Iode dans les urines. A l'accouchement, le sang était collecté du cordon ombilicale de l'enfant pour les testes de la fonction de la tyroide. La moyenne de l'excretion de l'Iode dans l'urine maternelle avait été significativement faible a Saki compare à Ibadan (144.76 ± 14.68 contre 213:36 ± 9.89ug/l, $P < 0.01$). Le taux total de goitre maternel (TGR) avait été de 26.6% et 1.1% à Saki et à Ibadan respectivement. Les moyennes totales de T_3 et T_4 dans le plasma maternel etaient relativement faible à Saki était relativement au dessus de notre interval de reference de laboratoire (0.3 – 0.5 mu/l) et plus élevé que les valeurs rencontre chez les mamans d'Ibadan (6.54 ± 1.58 contre 1.48 ± 1.37 mu/l, $P < 0.05$), quoique la difference n'etait pas aussi statiquement significative. La moyenne total du T_3 et T_4 neonatal etait plus faible a Saki compare a Ibadan, mais les differences n'etaient pas statiquement significatives. La moyenne de TSH du plasma a Saki etait au dessus de l'interval de reference des adultes et significativement plus eleve que le niveau observe a Ibadan (9.82 ± 1.64 contre 4.18 ± 1.17mu/l, $P < 0.05$). L'incidence de l'hypothyroidisme chimique neonatal (NCH) a Saki avait été de 14.7 par 1000 bébés. Aucun cas de NCH n'avait été observe à Ibadan. Ces resultats suggerent une deficience de l'iode environmentale et une hypotyroidisme chimique chez les meres et nouveaux nes de Saki comparé aux mères et nouveaux nés des regions n'ayant pas de deficience en Iode.

Introduction

Lack of iodine in the diet results in deficient production of the thyroid hormones, thyroxine (T4) and triiodothyronine (T3). Inadequate thyroid hormone production gives rise to the iodine deficiency disorders (IDD) [1]. This comprises goitre, hypothyroidism, still-births, miscarriages, and cretinism, as well as lesser degrees of loss of physical and mental function. These disorders affect the foetus, neonates, young children and adults.

Impairment of nervous system development and function is the most important consequence of iodine deficiency. In the developing human foetus, thyroid hormone deficiency is associated with severe retardation of growth and maturation of almost all organ systems [2]. The sensitivity of different organs to thyroid hormone deficiency varies. The brain is particularly susceptible to damage during foetal and early postnatal period.

It has been established that nerve cells require thyroid hormone for their development [3]. The developing foetus begins its own thyroid hormone production only after the 10th-12th week of gestation, and as estimated from plasma values, the thyroid hormone production becomes appreciable only in the 20th week. The formation of nerve cells precedes or coincides with the foetus' own thyroid hormone production. Experimental data show that, prior to foetal endogenous hormone production, development depends on the mother's thyroid [4,5,6]. Thyroid hormone deficiency (hypothyroidism) occurring during this period gives rise to the syndrome of cretinism, which is

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characterised by retardation of physical, neuromotor, auditory and intellectual maturation.

Endemic cretinism refers to the type of cretinism that is associated with endemic goitre and is seen in iodine deficient environments. Experimental data suggest that the neurological deficits of endemic cretinism result from severe iodine deficiency in mothers during pregnancy and that the effect of iodine deficiency is mediated through the combined effects of maternal and foetal hypothyroidism [4, 5, 6].

Previous studies in Saki have shown that this area is iodine deficient with significant IDD problems [7, 8]. Saki is the headquarter of Ifedapo Local Government Area of Oyo State in southwestern Nigeria. It lies towards the northern borders of the State, close to Kwara State in the north and the Republic of Benin in the west. It is a distance of 195 km. from Ibadan, the state capital. The vegetation is that of Guinea Savannah grassland with some scattered trees. The topography is hilly and rocky. Saki is semi-urbanized and thickly populated. The 1991 census estimated the population as 230,713. Saki lies in the extensive endemic goitre belt of Southwestern Nigeria, as described by Olurin in 1974 [7]. Apart from the earlier goitre prevalence surveys done by Olurin [7] between 1970 and 1974, no further evaluation of the IDD_s in this area has been undertaken to our knowledge. This study was therefore designed to assess the iodine and thyroid status of pregnant mothers and their neonates, with a view of further appraising the public health importance of IDD in this locality.

Patients and methods

One hundred and five (105) subjects from Saki and ninety (90) from Ibadan (a non-iodine deficient locality)were recruited into the study. The subjects were recruited form the ante-natal clinics of different health institutions in both Saki and Ibadan. All subjects were apparently healthy with non evidence of renal, hepatic, endocrine or other metabolic disease that would affect thyroid function and with at least 37 completed weeks of gestation. Each subject had resided in the locality for at least 24 months. All patients who met the inclusion criteria and were delivered of live babies within the study period were recruited into the study.

Each patient was thoroughly examined and assessed for goitre and blood sample obtained by venepuncture for thyroid function and tests before onset of labour. Spot urine samples were also obtained from the mothers at the time of examination for urinary iodine estimation. At the time of delivery cord blood samples were obtained from the neonate for thyroid function tests. Prior informed consent for recruitment into this study was obtained from the relevant local authorities and the patients.

Goitre was graded according to WHO/ICCIDD (World Health Organization/International Council for the Control of Iodine Deficiency Disorders) criteria (Grade 0 = no goitre; Grade 1A = goitre palpable but not visible; Grade 1B = goitre palpable and visible with neck extended; Grade 2 = goitre visible with neck erect; Grade 3 = goitre visible from about 10 metres). Plasma triiodothyronine (T3) and thyroxine (T4) were estimated by radioimmunoassay (R.I.A.) using standard commercial kits from Diagnostic Products Corporation, Los Angeles, California, U.S.A. T3 was done by double-antibody R.I.A. while T4 was by solid-phase coated tube (Coat-A-Count) R.I.A. methodology. TSH was estimated by immunoradiometric assay (IRMA) using coated tube methodology (Coat-A-Count).

Urine samples were assayed for their iodine content using the acid digestion method of IPCIDD (International Training and Support Programme for the Control of Iodine Deficiency Disorders, Center for Disease Control, Atlanta, Georgia, U.S.A.). This is based on the colorimetric ceric ion./arsenious acid/iodine catalytic reaction.

All results are expressed as mean ± SEM. Mean values for Saki (iodine-deficient) and Ibadan (control) subjects were compared by the unpaired Student's t-test, using the OXSTAT II programme on an IBM compatible Sanyo personal computer. The level of statistical significance was $p < 0.05$.

Results

Table 1 summarizes the characteristics of the study and control subjects. It shows that both groups were similar in terms of maternal age, maternal weight, maternal height, neonatal birth weight and neonatal birth length, hence values of the different parameters from the two groups should be directly comparable. Differences in these parameters between the two (2) groups were not statistically significant ($p > 0.05$).

Table 1: Characteristics of study and control (Mean ± S.E.M.)

	Saki n = 105	Ibadan n = 90
Maternal age (years)	28.14 ± 1.17	26.23 ± 0.76
Maternal weight (kg)	57.78 ± 1.14	54.95 ± 1.72
Maternal height (m)	0.60 ± 0.01	0.61 ± 0.02
Neonatal birth weight (kg)	1.04 ± 0.05	3.09 ± 0.08
Neonatal birth length (cm)	47.27 ± 0.46	47.48 ± 0.57

Table II summarizes the maternal and neonatal thyroid status indices and maternal urinary iodine concentration for the study and control subjects.

Table 2: Indices of thyroid status (Mean ± S.E.M.)

	Saki n = 68	Ibadan n = 30
Maternal total goitre (TGR)	46.8%	2.2%
Maternal visible goitre (VGR)	26.6%	1.1%
Maternal urinary iodine (μg/L)	144.76 ± 14.86	213.36 ± 9.89
Maternal urinary iodine (μg/L)	115.00	237.50
Maternal triiodothyronine (T3) (nmol/L)	2.10 ± 0.18	2.59 ± 0
Maternal thyroxine (T4) (nmol/L)	91.76 ± 3.98	95.98 ± 4.89
Maternal thyroid stimulating hormone (TSH) (mU/L)	6.54 ± 1.58	4.18 ± 1.37
Neonatal triiodothyronine (T3) (nmol/L)	0.45 ± 0.08	0.58 ± 0.10
Neonatal thyroxine (T4) (nmol/L)	81.34 ± 4.50	84.94 ± 3.86
Neonatal thyroid stimulating hormone (TSH) (mU/L)	9.82 ± 1.64*	4.18 ± 1.17
Neonatal chemical hypothyroidism (NCH) (per 1000)	14.7	0

*$P < 0.05$

Goitre rates

Goitre rates were much higher in Saki (iodine-deficient) than in Ibadan (non-iodine deficient). The total goitre rates (TGR) were 46.8% and 2.2%, while visible goitre rates (VGR) were 26.6% and 1.1%, respectively, in Saki and Ibadan. TGR includes goitre grades 1A, 1B, 2 and 3, while VGR includes only goitre grades 2 and 3. This result

constitutes good evidence of environmental iodine deficiency in Saki

Maternal urinary iodine

The urinary iodine concentration was significantly less in subjects from Saki when compared to subjects from Ibadan (144.76 ± 14.86 vs 213.36 ± 9.89) µg/L; $p < 0.01$). This conclusively shows that mothers in Saki ingested less iodine from their food and water than mothers in Ibadan, and constitutes further evidence of environmental iodine deficiency in Saki.

Maternal thyroid status

Both T3 and T4 for the study and control populations were similar and within the reference interval of our laboratory (T3 = 1.3-2.8 nmol/Ll T4 = 57.0-164.0 nmol/L). For both hormones, however, the levels were higher in subjects from Ibadan (non-iodine deficient) as compared to subjects from Saki (T3: 2.59 ± 0.15 vs 2.10 ± 0.18 nmol/L, $p > 0.05$; T4: 95.88 ± 4.89 vs 91.76 ± 3.98 nmol/L, $p > 0.05$. Maternal TSH was also higher in Saki subjects (6.54 ± 1.58 mU/L) when compared to Ibadan subjects (4.18 ± 1.37 mU/L), though the difference was not statistically significant. While the mean TSH level of the Ibadan mothers was within our laboratory reference interval (0.3-5.0 Uui/mL), the level in Saki mothers was above reference interval. The above results suggest that pregnant mothers in Saki may be relatively chemically hypothyroid when compared to pregnant mothers in Ibadan.

Neonatal thyroid status

Neonatal T3 and T4 were higher in Ibadan babies than in Saki babies (T3: 0.58 ± 0.10 vs 0.45 ± 0.08 nmol/L; T4: 84.94 ± 3.86 vs 81.34 ± 4.50 nmol/L), though the differences were not statistically significant ($p > 0.05$). The TSH was higher in Saki babies as compared to Ibadan babies (9.82 ± 1.64 vs 4.18 ± 1.17 mU/L) and the difference was statistically significant ($p < 0.050$).

These results suggest that babies born in Saki may also be relatively chemically hypothyroid when compared to babies born in Ibadan. However, only one baby born in Saki (out of 68 babies whose plasma hormone levels were assayed) could be classified as having neonatal chemical hypothyroidism (NCH), using the criteria of Kochupillai and Pandar [9], i.e., T4 < 38.6 nmol/L and TSH > 50 mU/L. This gives an incidence of NCH of 14.7/1000 in Saki. No baby born in Ibadan qualified to be classified as suffering from neonatal chemical hypothyroidism.

Discussion

Daily urine iodine excretion and iodine excretion from spot urine samples have been widely accepted as satisfactory indices of dietary iodine intake [10]. The mean urinary iodine excretion in any locality also reflects the environmental iodine status [11]. The mean maternal urinary iodine concentration in this study was significantly less in Saki when compared with Ibadan. Saki can therefore be said to be relatively iodine deficient. The TGR and VGR were significantly higher for Saki mothers when compared with Ibadan mothers. This most probably reflects the deficient iodine intake of Saki mothers due to environmental iodine deficiency. The disparity in goitre rates was probably further widened by the effects of pregnancy. During normal human pregnancy, renal clearance of iodine increases and plasma iodine falls [12]. Thyroidal clearance of circulating iodine shows a compensatory increase to maintain absolute levels of iodine uptake. The resulting increase in thyroid activity may be reflected by visible enlargement of the thyroid gland, particularly when dietary intake of iodine is low [12], as seen in Saki. The high goitre rates seen in pregnant Saki mothers are therefore not entirely surprising.

Maternal T3 and T4 levels in both Saki and Ibadan were within our laboratory reference interval, though absolute levels were slightly higher in Ibadan mothers. Maternal TSH level was higher in Saki than in Ibadan, with the Saki mean maternal TSH value being slightly higher than the upper reference interval of our laboratory. This pattern further suggests relative iodine deficiency in Saki, with euthyroidism being maintained in Saki by a compensatory higher TSH drive. The higher TSH drive probably also contributed to the higher goitre rates seen in Saki.

The neonatal thyroid hormone levels also generally reflected the pattern seen in the mothers. Neonatal T3 and T4 were similar for both groups, with the Saki mean values being slightly less than the Ibadan mean values though the differences were not statistically significant. The mean neonatal TSH value was however significantly higher for Saki (9.82 ± 1.64 vs 4.18 ± 1.17 mU/L, $p < 0.05$). There has been no dedicated study on cord blood and neonatal thyroid hormones for our local environment, to our knowledge. However, the plasma hormone levels seen in the babies used in this study reflect the pattern reported for other populations. At birth plasma T3 is known to be low, with high reverse T3 (r T3), due apparently to inhibition of 5' – deiodianse activity during the final stages of pregnancy and in parturition [13,14]. Cord blood thyroxine (T4) levels are known to be similar to those of the adult [13], as seen in our subjects. Low foetal thyroxine (T4) levels are also known to lead to a rise in foetal TSH, leading to thyroid stimulation [14]. Thus the lower T3 and T4 levels seen in Saki babies could have triggered the higher TSH levels seen in these babies.

TSH is a sensitive indicator of thyroid status [15,16] and reflects the thyroid status better than other thyroid function tests currently in routine use [17]. Our results thus suggest that pregnant mothers and babies born in Saki may have a poorer thyroid status and are relatively chemically hypothyroid when compared to pregnant mothers and babies born in Ibadan. This may have resulted from maternal iodine deficiency secondary to environmental iodine deficiency. Using the criteria of Kochupillai and Pandar (i.e., T4 < 3 µg/dl (38.6 nmol/L) and TSH > 50 mU/L (9), the incidence of NCH was 14.7/1000 in Saki and nil in Ibadan. While these criteria may not be entirely appropriate for this study since it was developed in a different geographical region of the world, it is reasonable to adopt them for now, even if they appear arbitrary, since we do not have any established figures for our local environment, to our knowledge.

The NCH incidence of 14.7/1000 neonates born in Saki further buttresses or earlier finding [8] that there is a significant IDD problem of public health importance in Saki, even though this may still be classified as being mild in severity. This finding is also consistent with that of Kochupillai and Pandar [9], who found a correlation between the incidence of NCH in areas with mild IDD problems (6-15/1000) and higher incidences in areas with more severe IDD problems (75 – 115/1000). Our result is also consistent with our unpublished observation of a high prevalence of cases of mental and neurological handicap in Saki, which necessitated the establishment of a school for

the handicapped in this town. This school had a large population of deaf and dumb and mentally retarded children, in addition to some blind and physically handicapped pupils. During our study in the town, we were also able to spot a cretin.

It has been observed that in serious iodine-deficient environments, in addition to the few clinically obvious cretins, a large number of individuals suffer from various lesser degrees of impairment of brain function due to intrauterine and neonatal hypothyroidism [9]. These include various degrees of impaired mental and motor function among the school children and the general population [13,18,19,20]. Consequently it has been suggested that the extent of such "subcretinous" brain damage in a given iodine-deficient environment be the most important criterion by which one should assess the health significance of iodine deficiency in an environment [9]. However, none of the conventional criteria used to assess the extent and severity of environmental iodine deficiency reflects this aspect of the health effects of iodine deficiency. The incidence of neonatal chemical hypothyroidism (NCH) is perhaps the only parameter which can reflect this serious but 'submerged' aspect of the health effects of environmental iodine deficiency [9].

The incidence of NCH has been shown to be a very sensitive index for assessing neonatal thyroid failure, and hence potential brain damage, in a given environment with iodine deficiency [9]. Preliminary data suggesting a high incidence of neonatal thyroid failure in iodine-deficient regions were presented by Thilly *et al.* in 1978 [21]. Other studies have subsequently confirmed the high incidence of NCH in iodine deficient regions [9,22]. These reports have therefore made the question of neonatal thyroid status in iodine deficient regions an important one needing urgent attention, particularly from the point of view of developing countries, for three reasons: (a) The number of people living in iodine-deficient environments in these countries amount to several hundreds of millions (over 150 million in Africa) [23]; (b)there are usually no routine neonatal thyroid screening programmes as practised in more developed societies; (c) it is well recognised that neonatal thyroid failure can result in irreversible brain damage if not corrected within the first three postnatal months.

The findings of a high maternal goitre rate and other anecdoctal evidences of the deleterious neurological effects of iodine deficiency in this environment are causes for concern. There may be other areas in Nigeria with worse IDD problems than Saki. The results of this study may just be showing the tip of the ice-berg. The need therefore arises for a comprehensive and complete mapping of Nigeria with regard to the IDD status of different localities, so that intervention programmes can be instituted in the worst affected areas. The need for routine neonatal thyroid screening in all third-world countries is over-due. The results of this study suggest the need for immediate intervention programmes in Saki.

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