REVIEW ARTICLE

Iodine Deficiency and Mental Performance: A Review

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ABSTRACT

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Introduction Iodine deficiency disorders (IDD) is responsible for a lot of adverse health effects and it is one of the most common causes of preventable mental impairment. Impaired cognitive function is an outcome of impaired neurodevelopment process during early pregnancy due to iodine deficiency.

Methods A few cross-sectional studies found differences in mental performance between areas with high iodine found naturally in the environment (well water) and those with low iodine level, but other studies showed otherwise.

Results Intervention studies with iodine also give variety of results ranging from significant improvement of mental performance to non-significant findings.

Conclusions Malaysia faces with challenges in iodine supplementation among the population but it can be dealt with effectively if the programme is well executed and monitored.

Keywords Iodine deficiency - Mental performance - Intelligence.

INTRODUCTION

Iodine deficiency disorders (IDD) is a serious global public health problem, where it has been estimated that 31.5% of school-age children (266 million) and 2 billion people among the general population[1] have insufficient iodine intake. Programmes to control iodine deficiency such as salt iodisation, have been effective for decades. However, iodine deficiency remains a major threat to the health and development of populations around the world, particularly among preschool children and pregnant women in low-income countries[2].

Dietary intake with low iodine is the most common cause of preventable mental impairment worldwide, which prompted a global drive to eliminate iodine deficiency through highly effective strategies of salt iodisation and iodine supplementation[3]. However, some national iodination programmes may have been ineffective in combating IDD because of widespread consumption of salt that has not been adequately fortified as well as by the presence of goitrogenic food sources being consumed in the environment[4].

MATERIALS AND METHOD

Indicator of Iodine Status

There are four indicators that are generally used in assessing iodine status; they are: i) urinary iodine concentration (UI), ii) goiter rate via thyroid size measurement, iii) serum TSH, as well as iv) serum thyroglobulin[5]. However, urinary iodine (UI) is considered as the indicator of adequacy of the iodine intake of the population. A reliable and practical technique in measuring iodine excretion is to measure the UI to creatinine level (UI/Cr) rather than measuring random spot UI concentration. Random spot sample is influenced by the day-to-day variability in iodine intake, water consumption of an individual, and in the amount of time it takes for iodine exposure to equilibrate[6]. In iodine sufficient areas, there will be day-to-day and within-day variations but in areas where there is mild to moderate iodine deficiency, the UI concentrations will have day-to-day variations. However, it is also worth noting that urine iodine measurement fluctuates based on a person's daily iodine intake and water consumption[3,4,6].

Effects of Iodine Deficiency

There are multiple adverse effects of iodine deficiency on human growth and development and iodine deficiency is still the most common cause of preventable mental impairment[7]. Effects of iodine deficiency depend on the degree of the deficiency and at what stage of life it occurs. The effects of iodine deficiency based on life stages can be summarized as in Table 1.

Table 1 Effects of iodine deficiency by age group

Age Group	Health Consequences of Iodine Deficiency
All Ages	Goiter, including toxic nodular goiter. Increased occurrence of hypothyroidism in moderate-to-severe iodine deficiency; decreased occurrence of hypothyroidism in mild-to-moderate iodine deficiency. Increased susceptibility of the thyroid gland to damage and thyroid cancer from iodine radioisotopes (e.g. from radioactive fall-out).
Fetus	Abortion Stillbirth Congenital anomalies Perinatal mortality
Neonate	Infant mortality Endemic cretinism
Child and Adolescent	Impaired mental function Delayed physical development
Adults	Impaired mental function Iodine-induced hyperthyroidism Overall, moderate-to-severe iodine deficiency causes subtle but widespread adverse effects in a population secondary to hypothyroidism, including decreased educability, apathy, and reduced work productivity, resulting in impaired social and economic development.

Source: Zimmermann[7]

Table 2 Relationship between iodine deficiency and mental performance

Country	Study Title, Publication Year	Subjects	Study Design	Outcomes measured	Tool Used to assess Cognition	Main Results	Reference
Malaysia	Micronutrients and its correlation with mental performance among the schoolchildren in Bario Sarawak: a preliminary study, 2003	25 schoolchildren aged 7-12 years	Cross sectional study	Mental performance	TONI2- (Test on Nonverbal Intelligence)	School children where higher content of iodine in the water wells perform better at school as compared to other isolated areas.	Zaleha et al.[15]
Bangladesh	Biochemical hypothyroidism secondary to iodine deficiency is associated with poor school achievement and cognition in Bangladeshi children. 1999	170 grade 1 and 2 children from severely iodine deficient areas	Matched cross sectional study	School achievement Cognitive and motor functions	1.Wide Range Achievement Test (WRAT) 2.Verbal fluency 3. Digit span 4. Visual search 5.French learning test 6. Corsi blocks 7. Ravens Coloured Progressive Matrices 8. Symbol modalities test 9. Modified stroop 10. Upper limb speed and dexterity 11. The Lafayette peg board	Euthyroid group had better scores in reading and spelling ($p< 0.001$) and mathematics ($p<0.01$) as compared to hypothyroid group. The euthyroid group had significantly better scores in the French learning test ($p <0.01$), but there was no group difference in any of the other cognitive or motor tests.	Huda et al.[16]
Mexico	Iodine deficiency and its association with intelligence quotient in schoolchildren from Colima, Mexico, 2008	303 children from public elementary schools	Cross sectional analytical study	Intelligent quotient	Raven's Progressive Matrices	IQ deficiency 4.26 times greater in those with moderate iodine deficiency ($p = 0.06$)	Pineda-Lucatero[4]
Spain	Intelligence Quotient and Iodine Intake: A Cross- Sectional Study in Children, 2004	1221 school children from Grade 1, 5 and 8.	Cross sectional study	Intelligent quotient	Cattel's test scale 1 and scale 2	The IQ was significantly lower in children who had urinary iodine levels less than 100 µg/ liter ($p < 0.01$) An IQ below the 25th percentile was significantly related to urinary iodine levels below 100 µg/liter (OR, 1.40; $p < 0.02$) and thyroglobulin values above 10 ng/ml (OR, 1.52; $P < 0.04$).	Santiago-Fernandez et al.[17]
Malaysia	Goitre prevalence and mental performance among Aborigines in Sinderut, Pahang, 1996	196 Aborigines aged 4-60 years old	Cross sectional study	Mental performance	Raven's test	No significant correlation between thyroid hormone levels and mental performance score ($r = -0.02$, $p = 0.8395$)	Zaleha et al.[20]
Albania	Iodine supplementation improves cognition in iodine-deficient schoolchildren in Albania: a randomized, controlled, double-blind study, 2006.	310 primary school children aged 10-12 years old	Double-blind intervention trial	Cognitive and motor performance	1. Raven's Coloured Progressive Matrices 2. Coding 3. Symbol Search 4. Digit Span 5. Rapid Object Naming 6. Bead Threading 7. Rapid Target Marking	Iodine treatment was associated with highly significant improvement in test scores on Raven's Coloured Progressive Matrices, rapid target marking, symbol search, and rapid object naming ($p < 0.0001$).	Zimmermann et al.[18]
Bangladesh	Cognitive and motor functions of iodine-deficient but euthyroid children in Bangladesh do not benefit from iodized poppy seed oil (Lipiodol), 2001	287 grade 1 and 2 students	Double blind randomized control trial		1. Verbal fluency 2. Digit span 3. Visual search 4. French learning test 5. Corsi blocks 6. Ravens Coloured Progressive Matrices 1. Symbol modalities test 2. Modified stroop 3. Upper limb speed and dexterity 4. The Lafayette peg board	No significant differences between treatment and placebo groups in any of the cognitive or motor function measures	Huda et al.[21]
Portugal	Psychomotor development of children from an iodine-deficient region, 2011	140 pregnant mothers, 86 children at day 3 of life, 12, 18 and at 24 months	Cohort	Child's level of development in the cognitive, motor and behavior domains.	Bayley Scale of Infant Development, converted to Mental Development Index (MDI) and Psychomotor Development Index (PDI)	Children born from mothers with FT4 levels <25th percentile (<10 pg/mL) had an OR of 2.1 for mild-to-severe delay.	Costeira et al.[11]
Malaysia	The supplementation of levothyroxine among indigenous people in endemic goitre areas : the impact of therapy, 1998.	311 at baseline, 323 at first visit, 256 during second, 239 during third and 184 during the fourth visit	Quasi experimental trial	Mental performance (after supplementation with 100µg thyroxine sodium).	Raven's Progressive Matrices	Significant increase in mental performance after 1.5 years of intervention	Zaleha et al.[19]

Iodine Deficiency and Mental Performance

Iodine is an important micronutrient that involves growth and development and it is an essential component of the thyroid hormones, thyroxine (T_4) and triiodothyronine (T_3)[8]. Normal neurodevelopment requires appropriate amount of T4. It is initially provided by the mother and, after mid gestation, by the maternal and fetal thyroids[9]. Major impact of thyroid hormones seems to occur during fetal life especially before the onset of fetal thyroid function, and it was also noted that iodine has its most significant effect if consumed by expectant mothers in sufficient amount during the early period of pregnancy[10,11]. Iodine deficiency during pregnancy and infancy may impair growth and neurodevelopment of the offspring and increase infant mortality. It can also cause stillbirths, abortions, and congenital abnormalities[5,7].

Thyroid hormone deficiency during the first and second trimesters of pregnancy would affect visual attention, visual processing, visuospatial skills and fine motor skills, whereas such deficiency during the second and third trimesters affects gross motor skills, memory and motor function[12]. Deficiency during childhood reduces somatic growth and cognitive and motor function.

Cognitive impairment has been recognized to occur in individuals who were diagnosed with hypothyroidism, a medical condition that is also associated with iodine deficiency, regardless of at what age the condition developed. While congenital hypothyroidism found to cause attention deficit, hypothyroidism in adult can cause deficit in memory, psychomotor delay as well as visuoperceptual and construction skill[13].

Studies have shown that populations affected by even mild iodine deficiency have their average cognitive capacity reduced, impaired school performance and lower intelligence quotient (IQ)[14]. A study carried out in Sarawak, Malaysia showed that school children who lived in a remote rural area where higher content of iodine in the water wells were found performed better at school as compared to other remote areas[15]. Those who were euthyroid had better cognitive function as compared to those found to be hypothyroid[16]. A study in Spain reported that there was a greater risk of children with urinary iodine levels less than 100 μg/liter to have IQ below the 25th percentile or even a clinically significant decreased in IQ showed an IQ of 70 or less[17].

Effects Of Iodine Intervention On Mental Performance

Several intervention studies were done to determine the effect of iodine supplementation on mental performance. Treatment with iodized oil was found to produce a marked and sustained improvement in iodine status and this resulted in improvement of mental performance in school children albeit small increase was seen[18]. Supplement with thyroxine sodium among Orang Asli in Malaysia also found to have positive effects on mental performance[19].

Other studies however showed no significant association between iodine deficiency and mental performance[20,21]. This can probably be explained that most of the studies of mental performance in children were unable to distinguish whether the effect of iodine deficiency is in utero or it is an effect from the current iodine status. As discussed earlier, significant effects on brain development by iodine happens during the early stage of pregnancy[18].

Malaysia Scenario And Challenges In Improving Iodine Deficiency

The findings from the National Iodine Deficiency Survey in 1996 lead to salt iodization programme in Sabah and Sarawak since 1999 but it was found that iodine deficiency was not a public health problem for Peninsular Malaysia. However, a more recent study showed otherwise where Orang Asli in Hulu Selangor were found to have moderate iodine deficiency with median UI of 45.1 μg/L as compared to the recommended level of at least 100 μg/L[22]. The 2008 IDD National Survey also showed that almost 50% of the states in Peninsular Malaysia had median UI of less than 100 μg/L[23](1). Poor iodine consumption by the population could be the reason of this deficiency. Although worldwide, the number of households using iodised salt has risen from less than 20% to more than 70%[5], only 17.6% of Malaysians consumed iodized salt that contains the recommended level of ≥ 15 ppm and only 6.8% populations of Peninsular Malaysia consumed the recommended level[23]. Study of the distribution of iodized salt as well as on the accessibility of iodized salt and other iodine fortified foods might give a true picture of iodine consumption pattern among the Malaysian population. Besides poor dietary intake of iodine, high consumption of goitrogens such as tapioca roots and leaves has been associated with high prevalence of palpable goitre in the native population in Sarawak[24].

Another way of delivering iodine to the community was through the fitting of iodinator into the existing gravity-feed water supply in the villages[25]. Water iodinator was used in Terengganu since 1997, but a study done in 2004 showed that although there was a significantly higher UI among school children where the school was fitted with water iodinator system, the consumption of the iodised water was very low where only 43.5% of the study subjects consumed it once a week[25]. Hence, any programme in combating IDD should

be reviewed and monitored regularly to ensure its success. A more vigorous campaign to instill awareness among the public about the adverse effects of IDD can possibly increase their compliance towards IDD intervention programmes.

CONCLUSIONS

Iodine deficiency is still a problem in many parts of the world despite the availability of iodination programmes in most countries. Factors such as inadequate fortification and unequal coverage of the programme should be looked into. Studying the local dietary habits might give a clue on what are the sources of iodine received and consumed by the local population as well as the type and amount of goitrogens in the local environment that can aggravate iodine deficiency. Tailoring programme based on local dietary consumption will be more beneficial to the target population especially in combating the adverse effects of iodine deficiency mainly on childrens' mental performance.

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