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# Excess Iodine and Reproductive System: A Mini Review

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## Abstract

Iodine deficiency has always been known to disrupt the physiological system of an organism. The most affected being thyroid gland. The other organ systems also bear the brunt but another acutely affected region is the reproductive system. Iodine deficiency disorders led to implementation of salt iodization programs throughout the world. Various countries took different measures to curb iodine deficiency. This caused indiscriminate consumption of iodine on a regular basis even in environmentally iodine replete regions. This often caused iodine accumulation in excess of the required dietary recommendations. In turn, it again affected the thyroid-reproductive axis irrespective of the sex. This excess iodine affects the male and female reproductive systems via separate mechanisms. Not only the organs themselves, but also the fertility rates were affected in these organisms. However, the ultimate effect of even excess indiscriminate iodine consumption appeared to be disruption in the reproductive function of the organism. The objective of this review is to outline the effects of excess indiscriminate iodine consumption on the reproductive system.

**Keywords:** excess iodine, male reproduction, female reproduction, ovary, testes

## Introduction

A trace element of the Earth's crust, iodine is an essential microelement required as an integral component of the hormones of the thyroid gland. The physiological effects exerted by the thyroid gland are on account of its two main hormones – triiodothyronine (T3) and thyroxine (T4). Biosynthesis of these two hormones requires the organification of iodide into the follicular cells of the thyroid gland[1]. It has been well established that iodine deficiency causes pathological alterations of the thyroid gland in adults, children, neonates and fetuses. Besides severe developmental defects in fetuses and neonates it further leads to alterations of body physiology affecting almost all systems regulated by thyroid hormones. These conditions are collectively termed as Iodine Deficiency Disorders (IDDs) which includes goitre, hypothyroidism, reproductive failure, child mortality, stillbirth and socioeconomic retardation[2]. In order to treat these IDDs, supplementation of iodine in the diet has been a major step through the Universal salt iodization programme. Besides providing an adequate supply of iodine in regions with iodine deficiency, consumption of iodine in regions which are environmentally iodine sufficient has led to an excessive intake of iodine over and above the recommended requirements[3].

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As deficiency of iodine affects the functional status of thyroid gland, similarly, when consumed in excess of its required level, iodine also causes disruption of synthesis of thyroid hormones. This in turn alters the physiology of the other systems of the body whose functioning is intricately regulated by the thyroid[4]. One such system is the reproductive system. The male reproductive system is known to be affected by exposure to excess iodine[5]. It is also well known that thyroid disorders are more common in females[6,7]. Ovary being the primary reproductive organ of the female reproductive system, its structure and function are regulated by the thyroid hormones through the hypothalamo-pituitary-thyroidal-gonadal axis. This axis not only regulates the ovarian steroidogenesis but also regulates the intricately delicate mechanism of ovulation[8]. Thus any disruption of the thyroid physiology would probably be instrumental in subsequent dysregulation of both the male and female reproductive physiology.

Excess iodine consumption may be varied, depending on the dosage. The studies conducted mostly used two separate doses, one within the tolerable range and other well above the tolerable range. The tolerable dose was one where the thyroid physiology is not affected and the serum levels of thyroid hormones remained normal. The other dose was where the thyroid physiology was also affected. It must be noted that both these doses were non-toxic[5,9,10].

**Excess iodine: Sources**

In order to curb IDDs universal salt iodization has been the most important source of excess consumption of iodine through the table salt. Besides iodine in the form of iodized oil is often administered orally and intramuscularly, introduced into the water supply, used in crop irrigation, incorporated into animal fodder and introduced as bread iodophors and other products[11]. Fortified micronutrient biscuits have also been successfully used to raise the median UICs of schoolgirls (aged 10–15 years) in India[12]. Other important sources include radioiodide use as a contrast media in radiology and diagnostic studies, various drugs like iodine tablets, amiodarone, etc, supplements like seaweeds constitute important sources of excess iodine. Beside these, various expectorants, food preservatives, prescribed medications, parenteral nutrition preparations, mouthwashes[13], vaginal douches[14] also contain iodine.Other rich sources among food items also include marine products like fish, shellfish, molluscs and, eggs and milk, as well as their derivatives.

**Excess Iodine and Male reproductive physiology**

Excess iodine in both the thyroid tolerable and non-tolerable doses were found to affect the male reproductive system. Accumulation of excess iodine in testes was found to generate ROS. This ROS brought about disruption in testicular function via two separate mechanisms. One, by inhibiting the activity of steroidogenic enzymes Δ5-3β Hydroxysteroid Dehydrogenase (HSD) and 17β-HSDs which in turn reduced the synthesis of testosterone. The decreased testosterone levels further brought about structural and functional changes in testes. The ROS generation was also found to affect the –hypothalamo-pituitary-adrenal axis, increasing corticosterone production, which in turn was found to downregulate testosterone production via inhibition of LH secretion[5]. SEM studies have also found excess iodine induced altered acrosomal integrity, seminiferous tubular structural deterioration, and apoptosis of spermatozoan cells with reduced male fertility[15]. Excess iodine also disrupted the spermatogenesis as well as blood-testis barrier via generation of oxidative stress, apoptosis and

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reduced spermatogenesis[16]. A study conducted on human population associated a decrease in semen quality in males with excessive iodine consumption[17]. Excess iodine has been reported to cause a decrease in the sperm count and also found to alter the mean weight of testis[18].

**Excess Iodine and Female reproductive physiology**

Iodine exposure in excess has long been associated with various reproductive pathologies in females. These include several carcinomas like breast, endometrial, ovarian, etc[19,20]. Excess iodine has been primarily known to disrupt thyroid physiology leading to either hyperthyroidism or hypothyroidism. THs receptors as well as TSH receptors have been found to be expressed in ovarian tissue[21]. Recent studies have also reported presence of NIS in testis[22] and have shown excess iodine induced altered testicular functions as well[5]. Hence the resultant hypo- or hyperthyroidism (as the situation may be) further caused a secondary effect on the reproductive physiology by bringing about various changes in the reproductive functions, thus disrupting the system[23]. Hypothyroidism has been associated with menorrhagia, anovulation, abortions, stillbirths, and premature births[24,25], whereas, hyperthyroidism has been known to cause amenorrhea, alterations in gonadotropin release and sex hormone-binding globulin (SHBG), and changes inthe levels and metabolism of steroid hormones in both females and males[24,25,26].

Previously studies had ruled out NIS expression as well as iodine accumulation in the ovary and/or uterus of humans as well as rodents. NIS has been only said to be restricted to thyroid gland, salivary glands, GI tract, mammary glands, etc. However, recent studies have reported not only the role of iodine itself in the development of follicles at various stages[8] but have also reported the expression and localization of NIS in ovary as well as uterus of humans as well as rodents[27].

The different doses of excess iodine were found to have different effects on the ovarian physiology. The tolerable doses although maintained a euthyroid status, but the accumulated iodine in ovary produced a hypoestrogenic state that altered the estrous cyclicity, steroidogenic enzyme activities, ovarian morphology as well as decreased fertility of the studied animals. The non-tolerable dose however produced a hyperthyroid condition, which consequently caused a hyperestrogenic state, ovarian hypertrophy, altered ovarian morphology, increased activity of steroidogenic enzymes, again altered estrous cyclicity, with decreased fertility of the animals. This study depicted a biphasic action of excess iodine at different doses[10,28].

**Excess iodine and Developmental changes**

Thyroid hormone deficiency from any cause at critical times of development may result in severe mental retardation, neurologic abnormalities, growth retardation, or abnormal pubertal development[29]. In humans ingestion of excessive iodine due to consumption of soy milk and seaweeds caused severe neonatal hypothyroidism[30]. An iodine-induced hypothyroid state can result in delayed or deficient brain and neuromuscular development of the newborn[31]. Exposure of a fetus to large amounts of radioiodine would result in thyroid tissue ablation and in similar delayed brain and neuromuscular development, if the hypothyroid state was not corrected (e.g., with hormone replacement therapy) after birth[32]. In one study, most young failed to survive for 24 hours and those that survived up to weaning, eventually no milk is

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found in their stomach and the histology of mammary gland showed the secretary capacity of the gland was lost[33].There have also been reports of reduced fetal survival with reduced lactation in rabbits, hamsters, swine and hens[34,35]. A study showed exposure to excess iodine during pregnancy and lactation induced hypothyroidism due to several epigenetic changes in the thyroid gland of male offsprings[36,37]. Another study depicted the toxic effect of excess iodine consumption in the form of potassium iodide. It was found to cause long-term irreversible neurotoxicity in male rats[38]. Another study associated excessive iodine intake during pregnancy with an increased rate of hyperthyrotropinaemia in neonates and their mothers[39].

## Conclusion

Universal salt iodization was introduced to curb the iodine deficiency disorders (IDDs). However, people residing environmentally iodine replete areas have been found to be exposed to excess iodine over and above the daily requirements. The studies conducted on the effects of excess iodine on the male and female reproductive system and the developing fetuses may be few but they point out the fact boldly that in tandem with iodine deficiency, iodine excess also disrupts the reproductive system either through oxidative stress, thyroid dysfunction or by directly affecting the organs themselves via iodine accumulation. As such, excess iodine consumption in any form needs to be regulated.

**Conflict of interest: NIL**

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