



Original Article

## Hypothyroidism and its associated factors after radioactive iodine therapy among patients with hyperthyroidism in the Northeast Coast State of Malaysia



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### المخلص

**أهداف البحث:** تهدف هذه الدراسة لتحديد حدوث قصور الغدة الدرقية والعوامل المرتبطة بها في غضون عام واحد بعد العلاج باليود المشع.

**طرق البحث:** أجريت دراسة بأثر رجعي بين المرضى الذين يعانون من قصور الغدة الدرقية الذين حصلوا على العلاج باليود المشع في عيادة الطب النووي، مستشفى جامعة ساينز ماليزيا، كلنتان. تم تضمين المعلومات الديموغرافية للمرضى، والجنس، وسبب فرط نشاط الغدة الدرقية، ووجود الأجسام المضادة، وجرعة العلاج باليود المشع واستخدام دواء ضد نشاط الغدة الدرقية بعد العلاج باليود المشع.

**النتائج:** من بين 167 مريضا تم فحصهم، تم ضم 137 مريضا للدراسة. كان معدل الإصابة بقصور الغدة الدرقية خلال عام واحد بعد العلاج باليود 32.9%. ووجد أن السيدات أقل احتمالا لحدوث قصور الغدة الدرقية بعد العلاج باليود المشع 0.406. وأن استخدام دواء ضد نشاط الغدة الدرقية بعد العلاج باليود المشع يرتبط بشكل كبير مع حدوث أقل لقصور الغدة الدرقية بعد العلاج باليود المشع 0.188.

**الاستنتاجات:** أظهرت الدراسة ارتفاع حالات الإصابة بقصور الغدة الدرقية خلال عام بعد العلاج باليود المشع. يرتبط الجنس واستخدام دواء ضد نشاط الغدة الدرقية بعد العلاج باليود المشع بشكل كبير مع حدوث قصور الغدة الدرقية.

**الكلمات المفتاحية:** قصور الغدة الدرقية؛ بعد العلاج باليود المشع؛ فرط نشاط الغدة الدرقية؛ مرض جريف

### Abstract

**Objectives:** The aim of this study was to determine the incidence of hypothyroidism and its associated factors within one-year post radioactive iodine (RAI) therapy.

**Methods:** A retrospective study was conducted among patients with hyperthyroidism who received RAI therapy at Nuclear Medicine Clinic, Hospital Universiti Sains Malaysia (HUSM), Kelantan. Data regarding patients' demographics, gender, aetiology of hyperthyroidism, presence of autoantibodies, dose of RAI used and usage of antithyroid drug post RAI therapy were included in the analysis.

**Results:** Of a total of 167 screened patients, 137 subjects were eligible for this study. The incidence of hypothyroidism within one year of RAI therapy was 32.9%. Women were found to be less likely to develop hypothyroidism post RAI therapy (adjusted odds ratio, 0.406; 95% confidence interval: 0.181–0.908;  $p = 0.028$ ). The usage of antithyroid drug post RAI was significantly associated with a lower incidence of hypothyroidism post RAI therapy (adjusted odds ratio, 0.188; 95% confidence interval: 0.081–0.438;  $p < 0.001$ ).

**Conclusion:** This study showed a high incidence of hypothyroidism within one-year post RAI therapy. Gender and usage of antithyroid drug post RAI therapy are significantly associated with the development of hypothyroidism.

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**Keywords:** Graves' disease; Hyperthyroidism; Hypothyroidism; Post radioactive iodine therapy

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## Introduction

Hyperthyroidism affects about 2% of women and 0.2% of men.<sup>1</sup> It is a hypermetabolic state characterised by elevated levels of free thyroxine (fT4) and/or free triiodothyronine (fT3) and a low level of serum thyroid stimulating hormone (TSH).<sup>2</sup> Weight loss, osteoporosis, atrial fibrillation, and embolic events are some of the complications associated with hyperthyroidism. The most profound effect of hyperthyroidism is on the cardiovascular system.<sup>3</sup> The causes of hyperthyroidism include toxic multinodular goitre (TMNG), toxic adenoma, and thyroiditis. However, the most common cause of hyperthyroidism is Graves' disease and the annual incidence of Graves' disease was found to be 0.5 cases per 1000 persons, with a peak incidence among persons aged 20–40 years.<sup>4,5</sup>

The proper treatment for hyperthyroidism depends on the identification of the symptoms and signs of the disease and its aetiologies. Antithyroid drugs, radioactive iodine (RAI) therapy and surgery are the main treatment modalities known to be effective. In 1941, RAI therapy was introduced and became popular due to its strong efficacy and safety profile.<sup>6,7</sup> The nuclide used in this therapy is iodine-131 (<sup>131</sup>I).<sup>8</sup> <sup>131</sup>I is a beta-emitting radionuclide with an average energy of 0.192 MeV (maximum energy of 0.61 MeV) and tissue range of 0.8 mm.<sup>9</sup> Although <sup>131</sup>I may cause cell mutation and cell death, all the iodine isotopes are rapidly taken up into the thyroid follicles; thus, only thyroid follicles undergo organification. The absorption and organification of <sup>131</sup>I beta radiation by the thyroid follicles result in the highly localised destruction of those follicles. <sup>131</sup>I disrupts thyroid hormone biosynthesis and causes the necrosis of the follicles and blood vessels. The half-life of <sup>131</sup>I is approximately 8 days and results in euthyroidism within 6–18 weeks.<sup>9</sup>

RAI therapy is indicated when antithyroid drug therapy fails to treat hyperthyroidism or when there is recurrent hyperthyroidism. Treatment of Graves' disease with medication is associated with 50–70% recurrence after completing a standard course of 1–2 years of antithyroid drugs.<sup>10</sup> Patients who are allergic to antithyroid drugs and who have neither TMNG nor thyroid cancer are the best candidates for RAI therapy. RAI therapy destroys the thyroid tissue and renders patients either euthyroid or hypothyroid.<sup>9</sup> Most often, hypothyroidism is a long-term effect of RAI that necessitates life-long thyroxine supplementation.<sup>8</sup> Hypothyroidism frequently develops in the first year after treatment. However, hypothyroidism may also manifest several years post RAI therapy.<sup>11</sup> Thus, patients who have undergone RAI require long-term follow up.

In Malaysia, RAI has become one of the main therapeutic services available at several tertiary hospitals and institutions

with nuclear medicine facilities. Hospital Universiti Sains Malaysia (HUSM) located in Kelantan, is the only facility that offers RAI in the Northeast Coast of Peninsular Malaysia where it serves as a referral centre for the two neighbouring states, i.e., Terengganu and Kedah. The RAI administration practice varies from centre to centre with regards to the selection of cases, preparation for RAI, dosage of radioiodine, and protocol for the use of antithyroid drugs pre- and post RAI. Although there are standard international guidelines for RAI therapy, the different practices may lead to different outcomes of RAI therapy from centre to centre, especially in the incidence of hypothyroidism post RAI therapy.

A study in Bangladesh showed that the incidence of hypothyroidism one year post RAI was 35.6%.<sup>12</sup> A retrospective study of 360 patients by Ghabhan et al. revealed that the incidence of hypothyroidism post RAI at 6 months and one year was 55.8% and 67.9%, respectively.<sup>13</sup> Ahmad et al. showed that the cumulative incidence of hypothyroidism was 55.8% at one year and 86.1% at 10 years.<sup>14</sup> There are many factors associated with the development of hypothyroidism post RAI therapy, such as history of Graves' disease, presence of thyroid autoantibodies, usage of antithyroid treatment prior to RAI and absence of a palpable goitre.<sup>13</sup> These conflicting results mandate further study regarding this issue. Thus, the objective of this study was to determine the incidence of hypothyroidism and its associated factors within one-year post RAI among patients with hyperthyroidism in the Northeast Coast Region of Malaysia.

## Materials and Methods

This was a retrospective record review study from 2002 to 2011. Patients were identified from the registered list of patients who underwent RAI therapy at the Nuclear Medicine Department, HUSM and were followed-up for at least one year after the therapy.

Patients with hyperthyroidism and older than 18 years, who received RAI therapy at the Nuclear Medicine Clinic and were followed up at the Endocrine Clinic in HUSM were included in the study. Patients' younger than 18 years and/or who were followed up for less than a year post RAI at the study centre were excluded from the study.

Patients' medical records and electronic data were reviewed. The socio-demographic data (i.e., age, gender and race) of all patients together with the aetiology of hyperthyroidism, date and dose of RAI therapy given, presence of autoantibodies, and post-therapy antithyroid drug usage were charted on the case report forms. The onset of hypothyroidism was determined by reviewing the results of serial thyroid function tests taken at one week and at every three months post RAI therapy up to one-year post RAI therapy. The subjects were grouped after all the available data were collected. The sample size calculation for the study yielded an optimal sample size of 167 after considering a single proportion, and a 10% drop-out rate (Ahmad et al., 2002).

At the centre, the dose of sodium iodide-131 (NaI-131) used in RAI was in the range of 5–15 mCi (185–555 MBq). The dose administered was based on the estimation of thyroid gland size by a trained endocrinologist during physical examination. Patients with small or normal thyroid glands

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