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Iodine deficiency and thyroid cancer trends in three regions of Thailand, 1990–2009

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ABSTRACT

Background: Iodine deficiency may play a role in thyroid cancer carcinogenesis. Because Thailand has region-specific historical iodine deficiency, it is ideal to evaluate the potential impact of recent national iodine supplementation policies on thyroid cancer incidence trends.
Methods: We examined thyroid cancer trends in Thailand from 1990 to 2009 in three geographically separated populations (Songkhla Province [south], Chiang Mai Province [north], and Khon Kaen Province [northeast]), each with a different historical prevalence of iodine deficiency. We used Joinpoint analysis and age-period-cohort (APC) models to investigate trends in thyroid cancer incidence.
Results: Pooled incidence of papillary cancers significantly increased (Males APC: 2.0, $p < 0.05$; Females APC: 7.3 [1990–2001, $p < 0.05$], −2.1 [2001–2009]) and incidence of follicular cancers significantly decreased (Males APC: −5.2, $p < 0.05$; Females APC: −4.3 [1990–1998, $p < 0.05$], 12.3 [1998–2001], −17.0 [2001–2005, $p < 0.05$], 8.2 [2005–2009]) in both males and females between 1990 and 2009. The largest increases in papillary cancer incidence, and the largest decreases in follicular cancer incidence, occurred in historically iodine-deficient regions. Interestingly, the significant histological changes coincided with Thailand's most recent national iodination policy. The thyroid cancer trends in females were better explained by period effects than cohort effects.
Conclusions: This study adds to the research indicating that papillary carcinoma incidence increases, and follicular carcinoma incidence decreases, as population-level iodine deficiency declines, and suggests that iodine exposure may affect late stages of thyroid carcinogenesis. However, our findings are limited by the ecological study design and lack of data prior to iodine supplementation.

1. Introduction

Thyroid cancer incidence is increasing worldwide [1,2]. In particular, it is among the most common cancers in the U.S., where incidence has increased dramatically over the last 35 years [1–3]. This increase has been largely driven by papillary thyroid cancers, which tripled in incidence in females between 1973 and 2010 and have been increasing at a rate of 6–7% a year since 1992 [3,4]. Papillary tumors are increasing more rapidly in females than in males in the U.S., and small papillary tumors are increasing more quickly than larger ones [1–3].

Because the incidence rate of thyroid cancer is more than twice as high in developed than developing countries, and because

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thyroid cancer mortality has remained stable despite increasing incidence [5–7], some theories attribute the rising incidence to increased screening or variations in diagnosis [1,3,8]. However, these theories are unlikely to fully explain international increases in thyroid cancer. Additionally, increases in large tumors and rising overall thyroid cancer incidence have also been observed in groups traditionally underserved by screening in the U.S. [3,4]. Therefore, unidentified risk factors are hypothesized to be contributing to the increase [2,4].

Exposure to ionizing radiation in childhood is the only widely accepted risk factor for thyroid cancer [8–10]. Some evidence has associated thyroid cancer risk with a variety of other factors, including family history, dietary nitrates, obesity, diabetes, and physical activity, but none has been conclusively shown to elevate risk [11–14].

Iodine deficiency is a potential risk factor for thyroid cancer. Goiter, which is commonly caused by iodine deficiency, is strongly associated with thyroid cancer risk [8]. Iodine deficiency appears to particularly elevate risk of follicular cancers, and residence in an endemic goiter region is associated with increased risk of follicular carcinoma [15,16]. Interestingly, some data suggest that high iodine intake does not reduce overall thyroid cancer risk and may even elevate risk of papillary carcinomas [8,17]. However, the evidence linking iodine supplementation to increases in papillary carcinomas is mixed. Though a number of country-level studies have reported an increase in the papillary:follicular carcinoma incidence ratio as well as an increase in papillary cancer incidence after the implementation of national iodine supplementation, a similar increasing ratio has also been observed in countries that did not introduce iodine supplementation [15].

Thailand presents a natural experiment to study the effects of iodine on thyroid cancer because of its heterogeneous history of iodine deficiency and recent iodine supplementation. Iodine deficiency, approximated by goiter prevalence, has historically been high in Thailand, particularly in the "Goiter Belt" of the north and northeast [18,19]. Studies in the 1950s and 60s reported high levels of endemic goiter and low urinary iodine in the northern, but not southern, regions [19,20]. Because iodine deficiency impairs cognitive development, the Thai government introduced iodized salt programs in the affected areas between 1965 and 1969, but distribution problems and decreased funding after the program's initial success led to a return of severe deficiency in some areas by the 1980s [19,21,22]. In response, in 1989 the Thai government began small-scale iodine supplementation programs in target provinces. From 1991–1995 iodized salt was again widely distributed, leading to a substantially reduced national prevalence of iodine deficiency and goiter [19]. Between 1993 and 1999, the total goiter prevalence in the north and northeast fell from 10 to 12% to around 3%, while in the south goiter prevalence fell from 4% to <1% of the population [18]. However, after 1999 governmental interest in iodine deficiency lessened. Between 2000 and 2005, median urinary iodine in pregnant women steadily declined below sufficient levels in north Thailand, while remaining below sufficient in northeast Thailand [18,23]. By 2005 median urinary iodine in pregnant women across15 target provinces again declined below sufficient levels [19], and deficiency was much more pronounced in the northern regions: 20–40% of Chiang Mai Province neonates had abnormal TSH in 2005–2006 [24], while only about 9% of neonates in Songkhla Province did in 2006–2007 [25].

Research in the early 1990s indicated that although papillary carcinoma was the most prevalent histological type in most of Thailand, follicular carcinoma was the most common histological type in Khon Kaen province (northeast), possibly due to the higher prevalence of iodine deficiency and goiter [26]. Interestingly, a recent prospective study in Khon Kaen, analyzing 17 cases diagnosed between 1990 and 2011, recorded more papillary than follicular cancers [27]. A separate cross-sectional study comparing regional registries confirmed that thyroid cancer incidence varies regionally, and the Songkhla province registry (in the south) recorded the highest thyroid cancer rates nationally in 2007 [28].

In these analyses, we examined trends in thyroid cancer in Thailand from 1990 to 2009 in three geographically separated Thai populations (Songkhla Province in the south, Chiang Mai Province in the north, and Khon Kaen Province in the northeast, Fig. 1). We hypothesized that papillary cancer incidence would increase, and follicular cancer incidence would decrease, as iodine deficiency decreased nationally in Thailand. Furthermore, we expected these trends to be particularly pronounced in areas known to be historically iodine-deficient. Finally, we examined the timing of histological trends in light of periods of national iodine supplementation, to assess whether supplementation affected population-level rates of thyroid cancer.

2. Materials and methods

2.1. Registries and case ascertainment

The Songkhla Registry was established in 1989 and actively extracts case data from community and private hospitals, the provincial health office, and the provincial population registration office. The Chiang Mai Registry was established in 1983 and actively extracts case data from all province public and private hospitals, as well as medical and pathology clinics [29]. The Khon Kaen Registry was established in 1987 and actively extracts case data from private and government hospitals, as well as health centers [30]. All three registries have been included in the International Agency for Research on Cancer's publication, Cancer

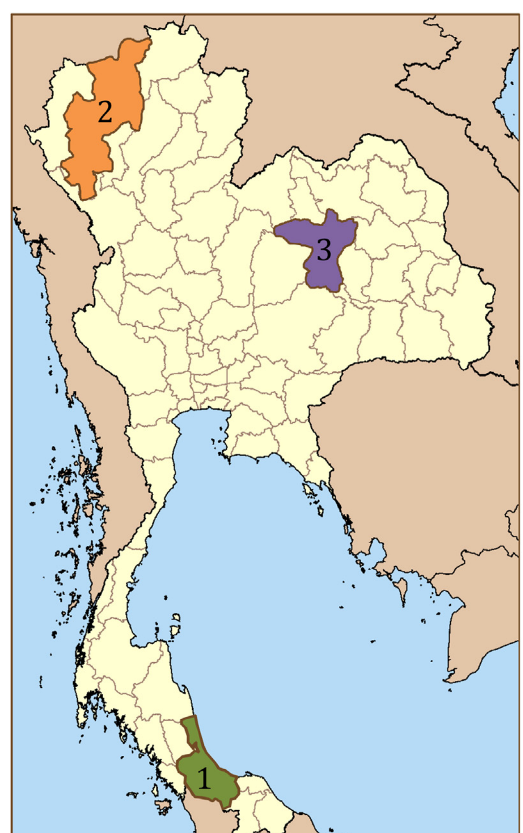

Fig. 1. Songkhla Province (1), Chiang Mai Province (2), and Khon Kaen Province (3), Thailand. Base map of Thailand created by Wikipedia contributor Ahoerstemeier.