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REVIEW ARTICLE

Incidence, Recurrence and Mortality Among Filipinos With Differentiated Thyroid Cancer: A Systematic Review

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Abstract

Background. The majority of thyroid malignancies are differentiated thyroid carcinomas (DTCs). We examined the incidence, disease extent, recurrence and disease-specific mortality (DSM) of DTC among Filipinos residing in the Philippines and Filipino immigrants.

Methodology. In accordance with the 2020 PRISMA statement, we performed a systematic literature search in MEDLINE, Google Scholar, EBSCO, Cochrane and Clinicaltrials.gov for the period January 1, 1980 until January 27, 2022. Pooled incidence rate ratio and pooled proportions of disease extent, recurrence and DSM were determined.

Results. Literature search yielded 1,852 studies. Out of 26 articles retrieved, nine retrospective case controls and cohorts were included. Incidence of DTC was significantly higher in female Filipino immigrants compared with non-Hispanic whites (NHW). Distant metastases and recurrence were more common among Filipinos and Filipino immigrants compared with NHW. Limited data showed higher DSM in Filipino immigrants and NHW than Filipinos, which may be influenced by reporting bias.

Conclusions. This review supports the trend of increased incidence and recurrence of DTC among Filipinos, although case registries are essential to confirm these findings. In the setting of the newly released Philippine guidelines for DTC, prospective studies with active long-term follow-up will help detect any changes in the outcomes of DTC among Filipinos.

Key words: Filipino, thyroid malignancy, differentiated thyroid carcinoma, papillary thyroid carcinoma, follicular thyroid carcinoma

INTRODUCTION

Thyroid cancer is the most common endocrine malignancy worldwide. Based on the Philippine 2020 Cancer Registry and Research Annual Report, it is the ninth most common malignancy.[1] The majority of thyroid malignancies are differentiated thyroid carcinomas (DTC), specifically papillary thyroid carcinoma (PTC) and follicular thyroid carcinoma (FTC), which have an indolent course, low risk of recurrence after treatment and favorable prognosis.[2]

Data on the incidence and prognosis of DTC in the Philippines are mainly derived from tertiary centers. The Philippine General Hospital, the largest referral hospital in the country, reported that PTC in Filipinos have almost twofold larger tumor size at presentation, two to seven times more frequent distant metastases at diagnosis, and two- to threefold greater recurrence compared with the Koreans and Japanese.[3]

The global trend of immigration has led to an increasing number of Filipinos all over the world. The Surveillance, Epidemiology and End Results (SEER) database comprises of data from Atlanta, Connecticut, Detroit, Hawaii, Iowa, New Mexico, Utah, New Jersey, Seattle-Puget Sound, San Francisco/Oakland, San Jose/Monterey, Los Angeles and all remaining areas of California, representing 54% of the Asian and Pacific Islander population in the US.[4] A review of the SEER database from 1973 to 1981 was the first to report that Filipino men and women have higher incidence rates of thyroid cancer. The average annual incidence of thyroid cancer was 7.3 per 100,000 for Filipino males and 17.3 per 100,000 for Filipino females, compared with 2.3 per 100,000 for Caucasian males and 5.4 per 100,000 for Caucasian females.[5] Similarly high incidence rates were noted in patients of Japanese and Hawaiian descent. Since then, multiple groups have investigated the effect of ethnicity, place of birth and immigration on the incidence, risk of recurrence and disease-specific mortality (DSM) of thyroid malignancy.

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Evidence-based management of DTC is guided by the 2015 American Thyroid Association (ATA) Management Guidelines for Adult Patients with Thyroid Nodules and Differentiated Thyroid Cancer. The latest recommendations discourage a single approach for all patients with DTC. Instead, treatment options and goals should be based on individual pre-operative characteristics and post-operative risk stratification.[6] Due to the increased incidence and higher risk for metastases and recurrence in Filipinos, some experts have deviated from the ATA recommendations and opt to have thyroidectomy done for thyroid nodules >1 cm in diameter regardless of the results of fine-needle aspiration biopsy.[7,8] The Philippine Interim Clinical Practice Guidelines for the Diagnosis and Management of Well-Differentiated Thyroid Cancer 2021 deviated from the ATA guidelines, primarily by recommending total thyroidectomy for all unifocal Bethesda category V and VI nodules exceeding 1 cm.[9]

In this systematic review, we examined the incidence rate, disease extent at diagnosis, recurrence rate, and DSM of DTC in Filipinos residing in the Philippines and other countries (Filipino immigrants) compared with other ethnic groups. The possible factors and mechanisms contributing to disease extent, recurrence and mortality of DTC in Filipinos were investigated.

METHODOLOGY

Search strategy and selection criteria

This review was performed according to the 2020 Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement.[10] This study was acknowledged by the Institutional Review Board. A systematic literature search until January 27, 2022, was performed in MEDLINE, Google Scholar, EBSCO, Cochrane, and Clinicaltrials.gov using combinations of the following keywords: "thyroid cancer" or "thyroid malignancy" or "thyroid carcinoma" and "*Filipino*" or "Philippines." We included cohorts and case control studies. No language restrictions were applied. Studies investigating PTC and FTC were included. Studies that included low-risk thyroid malignancy alone, anaplastic, medullary and other subtypes of thyroid malignancy were excluded. For studies involving Filipino immigrants residing outside of the Philippines, Filipino descent was defined as either birth in the Philippines or based on self-proclaimed primary race identification.

Data extraction and analysis

Two independent reviewers performed screening of titles and abstracts. Full-text articles of studies meeting all inclusion criteria were retrieved. Disagreements were resolved by consensus. Both reviewers assessed the risk of bias using the Newcastle-Ottawa Scale for cohort and case-control studies. Quality of the included studies were rated based on total score: poor quality for 0 to 2, fair quality for 3 to 5 and high quality for 6 to 9.

We extracted the following variables: ethnicity, incidence of PTC and FTC, presence of regional or distant disease at diagnosis, rate of disease recurrence or incomplete response and DSM. Incidence was reported per 100,000 person-years. The extent of disease at diagnosis or during primary surgery based on presence of lymph node metastases and distant metastases were obtained. Staging based on American Joint Committee on Cancer (AJCC) and ATA were not included due to changing definitions over the years.

StatsDirect Statistical Software 3.3.5 (StatsDirect Ltd) was used to determine the incidence rate ratio (IRR) between Filipino immigrants and non-Hispanic whites. Pooled proportions using the Stuart-Ord method was performed to compare the characteristics of thyroid malignancy in Filipinos, Filipino immigrants, and non-Hispanic whites. The fixed effects model (inverse variance) was utilized when heterogeneity based on I^2 is below 75%. When I^2 exceeds 75%, the random-effect model (DerSimonian-Laird) was used to achieve more conservative estimates of the 95% confidence intervals (CIs).

RESULTS AND DISCUSSION

Literature search yielded 1,852 studies. After removal of duplicates and screening of titles and abstracts, 26 articles were retrieved. Nine retrospective case controls and cohorts were deemed acceptable to be included in this systematic review. No randomized clinical trials were identified. The search flow diagram is presented in Figure 1.

Tables 1 and 2 summarize the characteristics of the included studies. The first group of studies was performed outside of the Philippines and contain data on the incidence and characteristics of thyroid malignancy in Filipinos

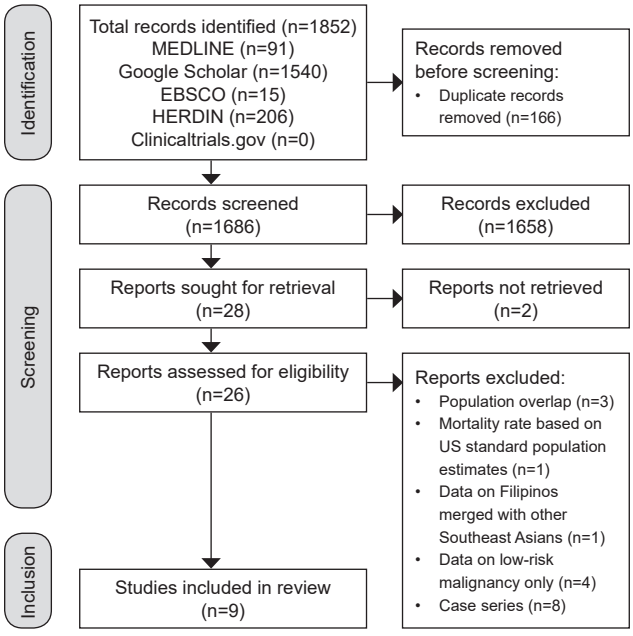

Figure 1. PRISMA flow diagram of search results.

who immigrated to other countries compared with non-immigrants or non-Hispanic whites (Table 1). The second group of studies was performed in the Philippines and present local data on the characteristics of DTC in Filipinos (Table 2).

The risk of bias of the included studies are summarized in Figure 2. All studies included were of fair to high quality. Only one study from the Philippines declared specific follow-up duration and presented DSM, which limits the analysis of disease outcomes.

Table 1. Characteristics of studies performed outside the Philippines

Study	Method	Source of data	Population
Clark 2006[7]	Retrospective, matched-pair analysis	Mount Sinai Hospital (Toronto) from 1983 to 2004	Filipino = 72 Matched control = 72
Kus 2010[8]	Retrospective cohort	Mount Sinai Hospital (Toronto) from January 1, 1984 to August 31, 2003	Filipino = 36 Non-Filipino = 463
Lee 2022[4]	Retrospective cohort	SEER* database from January 1, 1990 to December 31, 2014	Filipinos = 5,341 Non-Hispanic whites = 106,397 Non-Filipino Asians = 8,303
Megwalu 2021[38]	Retrospective cohort	California Cancer Registry from January 1, 2004 to December 31, 2015	Filipino = 2065 Non-Filipino Asian = 4327 Non-Asian = 30,181
Shah 2017[13]	Longitudinal cohort	Ontario healthcare system from January 1, 1997; observed until March 31, 2015	Southeast Asia = 203,361 East Asia = 364,288 Other Immigrants = 1,611,968 Nonimmigrants = 12,480,116
Spitz 1988[5]	Retrospective cohort	SEER* database from 1973 to 1981	Filipino = 193 Non-Hispanic white = 5,979 Puerto Rico Hispanics = 528 Blacks = 384 New Mexico Hispanics = 189 Chinese = 103 Japanese = 196

*SEER – Surveillance, Epidemiology, and End Results

Table 2. Characteristics of studies performed in the Philippines

Study	Method	Source of data	Population
Lo 2016[3]	Retrospective cohort	Philippine General Hospital from January 1990 to June 2014	Filipino = 728
Mendoza 2015[22]	Retrospective cohort	University of Santo Tomas Hospital from January 2007 to December 2011	Filipino = 225
Santiago 2021[21]	Retrospective cohort	Makati Medical Center from 2013 to 2017	Filipino = 115

	Selection				Comparability		Outcome			Total score	Quality
	Representative of exposed	Representative of non-exposed	Ascertainment of exposure	Outcome not present at start of study	Comparability of main factor	Comparability of additional factors	Assessment of outcome	Sufficient follow-up time	Adequacy of follow-up		
Clark 2006[7]*	★	★	★		★	★	★	★	★	8	High
Kus 2010[8]	★	★	★		★		★	★	★	7	High
Lee 2022[4]	★	★	★		★		★			5	Fair
Megwalu 2021[38]	★	★	★		★		★	★	★	7	High
Shah 2017[13]	★	★	★	★	★		★	★	★	8	High
Spitz 1988[5]	★	★	★		★		★			5	Fair
Lo 2016[3]	★		★				★	★		4	Fair
Mendoza 2015[22]	★	★	★		★		★		★	6	High
Santiago 2021[21]	★	★	★		★		★		★	6	High

*Modified NOS criteria for case-controls used

Figure 2. Newcastle-Ottawa Scale (NOS) risk of bias scoring of included studies.

Table 3. Incidence of differentiated thyroid cancer

Study	Filipino immigrants		Non-Hispanic whites	
	Male	Female	Male	Female
Papillary Thyroid Cancer				
Spitz 1988	5.2	12.5	1.5	3.9
Lee 2022	5.8	17.9	4.5	13.2
Pooled IRR	I^2 = 97.5% Random effects = 2.1 (95% CI 0.8 to 5.5), *p*=0.136	I^2 = 93.8% Random effects = 3.9 (95% CI 2.6 to 6.1), *p*<0.0001		
Follicular Thyroid Cancer				
Spitz 1988	1.0	4.0	0.4	0.9
Lee 2022	0.5	1.6	0.6	1.3
Pooled IRR	I^2 = 89.5% Random effects = 1.4 (95% CI 0.5 to 4.1), *p*=0.5581	I^2 = 0% Fixed effects = 3.8 (95% CI 3.4 to 4.3), *p*<0.0001		

Age-adjusted incidence rates reported per 100,000 person-years

Incidence of thyroid malignancy in Filipinos

In 2008, a nationwide survey estimated that 4.1% of Filipinos have nodular thyroid disease, although the etiology of these nodules were not identified.[11] We did not find a study on the incidence of DTC in the Philippines, but a report from the Philippine Cancer Society estimated that the age-adjusted incidence of thyroid malignancy was 3.4 per 100,000 person-years in males and 11.4 per 100,000 person-years in females from 2003 to 2007, with >90% of cases classified as DTC.[12]

We were able to find two retrospective studies from the United States (US) investigating the incidence of thyroid malignancy in Filipino immigrants compared with non-Hispanic whites (Table 3). Male Filipino immigrants had 2.1-fold (95% CI 0.8 to 5.5) higher incidence of PTC, although this was not significant (p=0.136). Among females, Filipino immigrants had significantly higher incidence of PTC with IRR of 3.9 (95% CI 2.6 to 6.1, p<0.0001) compared with non-Hispanic whites. Similar trends for incidence of FTC were noted, with Filipino immigrants having non-significant trend for higher incidence of FTC in males (IRR 1.4, 95% CI 0.5 to 4.1, p=0.5581) and significantly higher incidence of FTC in females (IRR 3.8, 95% CI 3.4 to 4.3, p<0.0001). A longitudinal cohort done in Ontario showed higher incidence of all histologic types of thyroid malignancy in Filipino immigrants with adjusted hazard ratio of 3.20 (95% CI 2.97 to 3.45) compared with non-immigrants.[13]

In a matched pair analysis of 72 Filipino immigrants and 72 non-Filipinos who presented with a thyroid nodule and underwent thyroidectomy, prevalence of DTC was 1.8-fold higher in Filipino immigrants (69.4%) compared with non-Filipinos (38.9%).[7] The incidence rate of DTC in Filipino immigrants in the US was almost 1.5-fold higher compared with the incidence of thyroid malignancy in Filipinos living in the Philippines. Filipino immigrants in the US also had a higher annual percentage increase in incidence of all subtypes of thyroid cancer (5.8%, 95% CI 2.9 to 8.7) from 2003 to 2010,[14] compared with an annual increase of 1.1% in males and 2.7% among females in the Philippines from 2003 to 2007.[12] These trends in incidence of thyroid malignancy may be due to under-reporting and low healthcare accessibility in the Philippines, in contrast to over-diagnosis of small, indolent tumors in developed countries.

Incidence of PTC and FTC were 2.4- to 3.1-fold higher in females compared with males across both ethnicities. Thyroid cancer is currently considered to be the only non-reproductive cancer with striking female predominance, with females having 3- to 4-fold higher incidence.[15] Although the exact molecular basis remains unknown, it is postulated that higher estrogen levels and higher risk for Hashimoto's thyroiditis may contribute to thyroid cancer pathogenesis in females.[16]

Using data from the California Cancer Registry from 1988 to 2004, Horn-Ross et al., found that the age-adjusted incidence rate of PTC was higher in Filipinas born in the US compared with Filipinas who were born in the Philippines then immigrated to the US (17.8 vs 13.3 per 100,000 person years, incidence rate ratio 0.7, 95% CI 0.6 to 0.9, p=0.02).[17] They postulated that the higher weight and body mass index in US-born Asian women may contribute to the increased risk for thyroid malignancy. The role of estrogen levels and parity on thyroid cancer risk remains to be determined.

Extent of disease at primary surgery

Characteristics of DTC in Filipinos were described in one study from the US, two studies from Canada, and three studies from the Philippines (Table 4). Pooled proportion of lymph node metastases during primary surgery was similar between the three groups: 0.3 (95% CI 0.2 to 0.4) in Filipinos, 0.3 (95% CI 0.3 to 0.3) in Filipino immigrants, and 0.3 (95% CI 0.3 to 0.3) in non-Hispanic whites. Distant metastases were reported in 0.1 (95% CI 0.03 to 0.2) of Filipinos, 0.03 (95% CI 0.02 to 0.03) of Filipino immigrants, and 0.02 (95% CI 0.01 to 0.02) of non-Hispanic whites.

AJCC and DeGroot staging systems were used in the studies. Presence of lymph node metastases upon initial surgery appears to be similar among Filipinos, Filipino immigrants and non-Hispanic whites. For PTC, which comprises 80% to 90% of all thyroid malignancies, 15% (range 5% to 34%) have extrathyroidal extension into adjacent soft tissues and 35% to 50% of excised neck lymph nodes have histologic evidence

Table 4. Extent of disease of well-differentiated thyroid malignancy in Filipinos, Filipino immigrants, and non-Hispanic whites

Study	Filipinos			Filipino immigrants			Non-Hispanic whites		
	Local	LN	Distant	Local	LN	Distant	Local	LN	Distant
Clark 2006				35/46	11/46	0/46	24/28	4/28	0/28
Kus 2010						0/33			
Megwalu 2021				1391/2065	614/2065	60/2065	21682/30181	8001/30181	498/30181
Pooled Proportions				0.7 (95% CI 0.6 to 0.7) I^2 = 33.4%	0.3 (95% CI 0.3 to 0.3) I^2 = 0%	0.03 (95% CI 0.02 to 0.03) I^2 = 25.8%	0.7 (95%CI 0.7 to 0.7) I^2 = 63.5%	0.3 (95% CI 0.3 to 0.3) I^2 = 52.9%	0.02 (95% CI 0.01 to 0.02) I^2 = 0%
Mendoza 2015	90/225	89/225	46/225						
Lo 2016	492/728	200/728	36/728						
Santiago 2021	88/115	18/115	9/115						
Pooled Proportions	0.6 (95% CI 0.4 to 0.8) I^2 =96.9%	0.3 (95% CI 0.2 to 0.4) I^2 =91.5%	0.1 (95% CI 0.03 to 0.2) I^2 =95.2%						

Table 5. Outcomes of well-differentiated thyroid carcinoma in Filipinos and Filipino immigrants

Study	Filipinos			Filipino immigrants			Non-Hispanic whites		
	Recurrence	Mortality	Follow-up	Recurrence	Mortality	Follow-up	Recurrence	Mortality	Follow-up
Clark 2006					0/46	32.3 ± 52.3 months			
Kus 2010				9/33 (0.3)		119.5 ± 53.4 months	44/463 (0.1)		
Megwalu 2021					101/2065	60 months		482/30181 (0.02)	60 months
Pooled Proportions					0.03 (95% CI 0.0005 to 0.09) I^2 = 75.7%				
Lo 2016	201/728 (27.6%)	4/728 (0.005)	62.4 ± 57.5 months						
Mendoza 2015	69/225 (30.7%)		At least 24 months						
Santiago 2021	47/115 (40.9%)		At least 24 months						
Pooled Proportions	0.5 (95% CI 0.02 to 0.9) I^2 = 99.7%								

of involvement.[2] Lymph node metastases at presentation of PTC do not seem to adversely affect survival, but it increases the risk of locoregional recurrence.[18] In contrast, FTC may have extensive local invasion but rare nodal metastases.[19]

Distant metastases were least frequent in non-Hispanic whites, followed by Filipino immigrants, and highest in Filipinos. In general, distant metastases are noted in 1% to 7% of patients at diagnosis of PTC[2] and 9.4% to 23% of FTC.[2,19] The higher rate of distant metastases in Filipinos compared with Filipino immigrants and non-Hispanic whites may be due to reporting bias towards more severe disease in the Philippines, since all data were reported by tertiary hospitals. Lack of access to healthcare services in the Philippines may have also contributed to these findings.

Recurrence after primary treatment

Recurrence was defined as the presence of biochemical or structural incomplete response and indeterminate response at least 2 years after thyroidectomy with or without radioiodine ablation. Disease recurrence was highest in Filipinos (pooled proportion 0.5, 95% CI 0.02 to 0.9), followed Filipino immigrants (0.3), and lowest in non-Hispanic whites (0.1) (Table 5).

In PTC, recurrent disease occurs in up to 30% of patients during the first ten years after treatment.[20] Management consists of thyroid surgery and radioactive iodine ablation (RAI). Extent of thyroidectomy and use of postoperative ablation varied among the studies included and may have affected the recurrence rate reported. For the studies done in the Philippines, RAI was done in 64%,[3] 80%,[21] and 100%[22] of patients. RAI significantly decreased recurrence in one study (OR 0.4, p<0.001)[23] but did not significantly affect recurrence in another study.[21] In the retrospective study by Kus, Filipino immigrants were found to have increased risk of thyroid cancer recurrence compared with non-Filipino patients (OR 6.9; 95% CI 2.3 to 21.1; p<0.001), even after controlling for sex, age, history of head and neck radiation therapy, family history of thyroid cancer, tumor size, tumor pathologic findings, stage of primary disease, use of radioactive iodine therapy, use of external beam radiation therapy and type of thyroid surgery.[8]

Disease-specific mortality

We found limited data on DSM. Mortality was highest in Filipino immigrants (pooled proportion 0.03, 95% CI 0.0005 to 0.09), followed by non-Hispanic whites (0.02), and lowest in Filipinos (0.005) (Table 5).

In general, patient survival in well-differentiated thyroid malignancy is excellent. Using data from the Multiple Cause of Death File of the National Center for Health Statistics of the US from 2003 to 2012, Nguyen et al., found that Filipino immigrants had significantly higher age-adjusted mortality rate due to thyroid cancer compared with non-Hispanic whites (1.7, 95% CI 1.5 to 1.9 vs 1.2, 95% CI 1.2 to 1.2 per 100,000 individuals, $p<0.0001$) and non-Filipino Asians (vs 1, 95% CI 0.9 to 1.1 per 100,000 individuals, $p<0.0001$). Furthermore, proportional mortality ratio compared with non-Hispanic whites was significantly higher for Filipino immigrants born in the Philippines than US-born Filipino immigrants (4.1, 95% CI 3.6 to 4.6 vs 2.6, 95% CI 1.6 to 4.1, $p<0.0001$).[24] The lower mortality rate from local Philippine data may be due to reporting bias, since Lo included patients with incomplete data,[3] such that patients lost to follow-up due to death from thyroid malignancy may not have been accounted for.

Environmental, genetic, and epigenetic mechanisms of disease

At present, we still do not know why Filipinos have higher incidence of DTC, higher disease recurrence and higher mortality rate compared with other ethnicities. Some studies suggest high iodine diet and possible radiation exposure in Filipino healthcare workers as possible mechanisms.[24] Environmental factors unique to the Philippines are yet to be investigated.

The genetic and molecular basis of thyroid malignancy have received much attention in recent years. Mutations in drivers of the MAPK signaling cascade, such as BRAF (MAP3K), RAS (small GTP-binding protein) and RET (receptor tyrosine kinase) have been identified as the main drivers of thyroid malignancy.[25] BRAF activating mutations account for 51% to 59.7% of PTCs and are strongly correlated with poor clinicopathological outcomes, such as extrathyroidal extension and lymph node metastasis, hence resulting in increased recurrence and mortality rates.[26] In Filipinos with conventional PTC, BRAF V600E mutations were found in 38.5%[27] and 70.6%.[28] Among Filipino immigrants in Hawaii with conventional PTC, 83.8% harbored the BRAF V600E mutation.[29] These rates are comparable with similar studies done in the US (50% to 88.2%),[30,31] Italy (37.5% to 62.2%)[32] and South Korea (79.7%).[33]

A group from California compared miRNA expression profiles of Filipino immigrants and European immigrants diagnosed with PTC. Compared with European immigrants, Filipino immigrants had significantly upregulated miR-4633-5p and significantly downregulated miR-491-5p and let-7. Higher miR-4633-5p have been associated with advanced thyroid cancer staging, while miR-491-5p and let-7 are tumor suppressors.[34] These findings suggest possible mechanisms for increased thyroid cancer incidence, distant metastases and recurrence in Filipinos.

Implications for management

The ATA has recommended a Risk of Recurrence Stratification System using tumor characteristics during initial surgery to guide aggressiveness of management of DTC. Patients are designated as low risk, intermediate risk, or high risk for disease recurrence based on the presence of extrathyroidal extension, vascular invasion, cervical lymph node metastases, distant metastases, incomplete tumor resection, tumor histopathology and postoperative thyroglobulin values.[6] In three studies from the Philippines, recurrence of PTC and DTC was significantly associated with multifocality, lymphovascular invasion, ATA high-risk stratification and detectable post-operative thyroglobulin and anti-thyroglobulin levels.[21–23] In Filipinos with DTC who underwent total or near-total thyroidectomy with post-operative RAI, incomplete response was noted in 8.3% of ATA low-risk patients, 53.7% of ATA intermediate-risk patients and 92.3% of ATA high-risk patients. Similar studies in the US and South America showed recurrence in 12% to 22% of ATA low-risk patients, 37% to 48% in ATA intermediate-risk patients and 69% to 84% in ATA high-risk patients.[35–37]

The higher incidence of DTC in Filipinos and Filipino immigrants suggest that thyroid nodules may need to be managed more aggressively in this ethnic group. Furthermore, the risk of disease recurrence appears to be higher than predicted by the ATA risk stratification system. Local data regarding DSM in Filipinos are still lacking. Additional prospective studies on the outcomes of thyroid malignancy in Filipinos are needed to provide definitive data on whether more aggressive treatment approaches are warranted in this ethnic group.

CONCLUSION

This systematic review supports the trend of increased incidence and recurrence of DTC among Filipinos and Filipino immigrants. This initial work can provide the basis for case registries that can give more comprehensive data on the incidence and prevalence of DTC in the Philippines. There is a need to evaluate the applicability of American Thyroid Association and European guidelines for thyroid cancer, in terms of risk assessment and appropriate management. In the setting of the newly released Philippine guidelines for thyroid carcinoma, prospective studies with active long-term follow-up is essential to detect any changes in the outcomes of DTC among Filipinos.

Limitations

Most studies included in this review are retrospective and are at high risk for reporting bias. Selection and attrition bias, especially in the studies conducted in the Philippines, may result in underreporting of extent of disease, recurrence and mortality. Studies included had heterogenous populations. Publication bias may have limited this review as well.

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Statement of Authorship
The authors certified fulfillment of ICMJE authorship criteria.

CRediT Author Statement
MDSJ: Conceptualization, Methodology, Investigation, Data Curation, Writing – original draft preparation, Writing – review and editing, Visualization; **EPP:** Conceptualization, Methodology, Data Curation, Writing – review and editing, Supervision

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