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Posted Date: 22 December 2023

doi: 10.20944/preprints202312.1721.v1

Keywords: goiter, Druze, Israel



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Article

Goiter Prevalence among Druze population in Northern Israel

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Abstract: Introduction: Goiter is one of the most common thyroid disorders, yet its etiology is still not completely understood. Previous studies suggested a possible genetic predisposition in combination of environmental factors. The importance of an ethnic hereditary factor in goiter prevalence has rarely been studied. Israel has a diverse ethnic composition: Jews, Muslim and Druze. A previous study of the Israeli Druze has demonstrated that they are genetically a population isolate. The prevalence of goiter in the Israeli Druze has yet to be studied. **Objectives:** The purpose of this study is to examine goiter prevalence in the Druze population of northern Israel compared with Jewish and Muslim populations in the same region. **Methods:** A retrospective study of adult patients presented with goiter to the head and neck clinic in Ziv medical center between 2019-2021. Only patients from the same geographical area were included in the analysis. Patient files were reviewed for their demographic data and other goiter related clinical characteristics. **Results:** A total of 392 patients were included in the study. Of the reviewed files 235 were Jewish, 123 Druze and 34 Muslims. The overall incidence of goiter in the Druze group was 6.92% (CI 5.75-8.25) compared to 4.11% in the Jewish (CI 3.60-4.67) group and 7.21% (CI 4.99-10.08) in the Muslim group. **Conclusions:** Goiter prevalence in the Druze population is higher compared to the Jewish population in northern Israel. Further studies of possible genetic factors are warranted. A larger study of goiter in the Israeli Muslims is also warranted.

Keywords: goiter; Druze; Israel

Introduction

Thyroid goiter is primarily benign and affects approximately 7% of the worldwide population, and is more common in women (1). (2). A normal thyroid gland is approximately 4 to 4.8 x 1 to 1.8 x 0.8 to 1.6 cm in size, with a mean sonographic volume of 7 to 10 ml and weight of 10 to 20 grams (3; 4). Goiter is defined as enlargement of the thyroid gland which is classified as diffuse with overall enlargement of the thyroid, or nodular as a result of irregular cell growth that forms nodules. These are further subdivided into toxic and non-toxic (5).

The symptoms and signs associated with a goiter depend on the size and location of the goiter. Direct compression of the trachea or esophagus by the goiter can cause worsening dysphagia with solids, positional dyspnea, and dysphonia. Other possible symptoms are shortness of breath and globous sensation (6). The standard work-up of goiter patients includes measurement of TSH, fT3, fT4, ultrasound imaging and fine-needle aspiration biopsy of nodules - according to the ATA guidelines (5; 7). Surgical removal of the thyroid in case of suspected malignancy in goiter, mechanical compression symptoms or for esthetic reasons (8). Other treatment options depend on the pathogenesis of the goiter and includes dietary iodine supplementation (in patients with iodine deficiency), radioiodine therapy (to decrease thyroid mass), and mini-invasive ablation techniques (7).

Although goiter is one of the most common thyroid disorders, its etiology is not completely understood. Multiple factors have been associated with goiter development. Environmental factors that were implicated as contributing to goiter development include low dietary iodine intake and tobacco use (9; 10). Additional factors include female gender, age, and high body mass index. However, even in endemic areas, environment cannot alone account for the development of simple goiter. It is suggested that other factors exist, that predispose a part of the population to goiter development (11).

Previous studies support the involvement of a genetic factor in the development of goiter. Clinical observations have suggested that goiter disease may evolve on a background of genetic predisposition, in combination with environmental factors (5). A study of twins concluded that the heritability of the predisposition to develop goiters is about 82% with only 18% explained by environmental factors (12). A genomic research of a Canadian family has identified a locus on chromosome 14q has as a possible cause for the disease (13). A study in Denmark has found a greater overlap of thyroid volume in twins which was attributed to genetic factors (14), another study in 2011 has found 4 genetic loci that were associated with thyroid volume (15; 16).

The importance of ethnic hereditary factors in relation to goiter prevalence has not been studied, with an exception of a study regarding the Efe Pygmies from 1989 (17), and a study in 1993 of Ethiopians who immigrated to Israel (18). Both studies have concluded that the major factors in the pathogenesis of endemic goiter in the studied populations are mainly genetic.

The country of Israel is unique in its diverse ethnic composition: Jews, Muslims, Christians and Druze. This unique condition allows research to enlighten the genetic factor. These ethnic groups are not mixed for religious, historical and cultural reasons.

The Druze are religiously an isolated community which resides partly in Lebanon, Syria and northern Israel. The Druze population has a unique historical, social and demographic structure, which is closely connected with their religion. Privacy from the outer world and a sense of community are important in the lives of the Druze. They reside in close-knit communities and maintain strong relationships that traverse the locality of villages to constitute an active network of brotherhood and sisterhood (19). The Druze have lived for decades in relative seclusion and have maintained a status of relative secrecy because of a long history of persecution. Furthermore, unlike other monotheistic religions, the Druze strictly close their religion to new adherents, thus preventing mixture with all other ethnic groups in the area. In a study of the phylogenetic mitochondrial haplogroup of the Galilee Druze it was demonstrated that they are a population isolate (20). As a result of the above mentioned, it is highly possible that the unmixed Druze population has a higher inclination for genetic diseases (21). The Israeli Druze population was estimated to be 150,000 persons in 2021 (22), and is distributed over three geographical sub regions: The Carmel, the Galilee, and the Golan Heights – all in the northern part of Israel (23). The majority of the Israeli Druze live in 11 towns and villages, 4 of these villages are located in the vicinity of the Ziv Medical Center in Safed. The Ziv Medical center is a medium size regional hospital, located in the northern part of Israel. The population it serves includes 3 major ethnic groups: Jews, Muslim and Christian Arabs and Druze. Patients from these 4 villages are primarily referred to Ziv Medical Center as it is the only large Medical Center in the area.

The aim of this study was to evaluate the prevalence of goiter in the Druze community residing in northern Israel, in comparison to the Jewish and Muslim population from the same geographic vicinity.

Methods

A retrospective study. We reviewed all adult patient's files presented with goiter to the head and neck clinic in Ziv medical center between 2019-2021. To limit differences of environmental factors among groups, we only included patients who reside in the same geographical area of hospital's catchment. The Druze group included only patients from the 4 Golan villages: Ein Kinia, Masade, Buqata and Majdal Shams. Jewish patients included were from Hatzor Haglilit, Kiryat Shemona, Safed and Katzrin. The Muslim Arab group included patients from Tuba-Zangariya village. These locations were selected because each is inhabited exclusively by a single ethnic group (Jewish, Arab-Muslim or Druze), and are all located in the same geographical area. The water sources supplying these locations were comparable, with Iodine levels of 4-6 µg/L.

Patient Data Collection

For each patient we collected the following data: goiter type, Bethesda score of fine needle aspiration cytopathology (FNAC), goiter related symptoms, ethnicity, place of residence, age, gender and family history.

Demographic Data Collection

Demographic data of all locations – the number of adult persons living in each location, was obtained from the Israel Population & Immigration Authority, (https://data.gov.il/dataset/residents_in_israel_by_communities_and_age_groups, accessed July 2022).

Statistical Analysis

In our analysis, continuous data are described using means and standard deviations. Categorical data are described using frequencies and percentages. The comparison of numeric data between groups was performed by an independent sample t test. Relationships between categorical variables and sample groups were examined using Chi-square test or Fisher's exact test depending on the sample size. Standardized Incidence Ratio higher than 1 was considered higher than expected and a P-value lower than 5% was considered statistically significant. The data were analyzed using the SPSS software, version 25 (SPSS Inc., Chicago, IL, USA).

Results

A total of 674 Goiter patients' files were reviewed for their demographic data and other goiter related clinical characteristics. 392 patients met the inclusion criteria and were included in the final analysis (Table 1). Among the included files 235 were Jewish, 123 Druze and 34 Muslims. The total overall mean age was 57.9, with 82.7% of the patients were females (p-value 0.562). The most common type of goiter was MNG type – nontoxic with 54.6% (p-value- 0.324). With the second most common being nodular nontoxic goiter with 40.1 (p-value 0.714). Family history was highest among Muslim patients 17.6 (p-value 0.006). Other variables are presented in Table 1.

Table 1. Demographic and clinical characteristics of the study patients stratified by ethnicity groups (#).

Variables	All patients (n=392)	Jewish (n=235)	Druze (n=123)	Muslim (n=34)	P
Age, years (M [95%CI])	57.9 [56.5-59.3]	59.8a [58.0-61.6]	56.5b [54.1-58.8]	49.7c [45.5-53.9]	<0.001*
Gender (n, %)					
Female	324, 82.7	191, 81.3	103, 83.7	30, 88.2	0.562
Male	68, 17.3	44, 18.7	20, 16.3	4, 11.8	
Bethesda score,1-6 (M [95%CI])	2.2 [2.1-2.3]	2.3 [2.1-2.4]	2.1 [2.0-2.2]	2.4 [2.0-2.8]	0.388*
Family history of Goiter (n, %)	23, 5.9	13, 5.5	4, 3.3	6, 17.6	0.006
Surgery (n, %)	65, 16.6	38, 16.2	15, 12.2	12, 35.3	0.006
Diffuse (n, %)	8, 2.0	5, 2.1	2, 1.6	1, 2.9	0.998
Nodular (n, %)	157, 40.1	98, 41.7	46, 37.4	13, 38.2	0.714
Multi-nodular (n, %)	214, 54.6	122, 51.9	74, 60.2	18, 52.9	0.324
Toxic (n, %)	12, 3.1	9, 3.8	1, 0.8	2, 5.9	0.171
Papillary carcinoma (n, %)	16, 4.1	12, 5.1	2, 1.6	2, 5.9	0.241
Difficulty swallowing (n, %)	56, 14.3	31, 13.2	17, 13.8	8, 23.5	0.269
Difficulty breathing (n, %)	54, 13.8	31, 13.2	16, 13.0	7, 20.6	0.483
Aesthetic problems (n, %)	14, 3.6	10, 4.3	2, 1.6	2, 5.9	0.363

* Kruskal-Wallis non-parametric test; # The Jewish group included patients from four towns, the Druze group included patients from four villages, Muslim group included patients only from one village. All are nearby residencies. a-c: different letters represent significant differences between the means.

The overall incidence rate of goiter cases divided by their respective population (residents over the age of 18) x1000 is presented in Table 2.

Table 2. Incidence rate calculations of Goiter stratified by ethnicity.

Ethnic group	Population (§)	Sample		Incidence	
	Residents over the age of 18 (n)	Patients with Goiter (n)	Patients with Goiter (%)	(Goiter cases / population) *1000	95% CI for Rate [#]
Druze	17,779	123	31.4	6.92	5.75-8.25
Jewish	57,150	235	59.9	4.11	3.60-4.67*
Muslim	4,715	34	8.7	7.21	4.99-10.08
Total	79,644	392	100		

§ updated to December 31st, 2021 according to the Israeli Population and Immigration Authority records. *Significant difference from the Druze group using OpenEpi, Ver. 3.01 with Person-Time=1, *significant differences between the control group and other two groups (p<0.01).

The observed number of patients having goiter in comparison with the expected value of Goiter and the Standardized Incidence Ratio (SIR) for each group is presented Table 3.

Table 3. Standardized Incidence Ratio (SIR) calculations of Goiter stratified by ethnicity.

Ethnic group:	Number of patients				
	Observed	Expected [§]	Residual	SIR [§]	95% CI for SIR
Druze	123	87.4	35.6	1.41	1.18-1.67
Jewish	235	281.1	-46.1	0.84	0.73-0.95*
Muslim	34	23.5	10.5	1.45	1.02-2.00
Total	392	[#] p<0.001, $\chi^2_{(2)} = 26.70$			

§ Expected value = 392 * percentage of residents over the age of 18 at each ethnicity group. # Chi-square for goodness of fit; § The Standardized Incidence Ratio (SIR) = Observe / Expected; *significant differences between the control group and other two groups (p<0.05).

Discussion

This is the first study to examine goiter prevalence in specific ethnic populations in the Northern District of Israel. Our results show an increased prevalence of Goiter in the Druze population with SIR value of 1.41 (1.18-1.67) compared to the Jewish population - 0.84 (0.73-0.95). These results suggest a possible genetic tendency of the Druze population for the development of goiter disease.

Goiter is considered a complex disease caused by genetic factors interacting with non-genetic factors such as iodine deficiency, cigarette smoking, obesity and gender (24). A strong genetic predisposition has been indicated by family and twin studies (25).

Targovnik et al. (2010) identified 50 mutations linked with goiter and hypothyroidism or euthyroidism that confirms the allelic heterogeneity of the thyroid gene mutations (26).

Multiple studies of familial inheritance of goiter exist, but very few studies have regarded the possibility of an ethnic tendency (27).

The Druze patients in our study are all from the 4 Druze villages located in the Golan Heights in northern Israel. It is suggested according to historical records that the origin of the Druze in each of these regions is different. Druze customs strongly favor marriage within the same village or the same geographical area. This social structure has turned the Druze into transnational isolates – a population which remains genetically isolated largely through the social practice of endogamy and consanguinity.

Two previous studies support this theory. Schaffer et al. (2017) has found an unusually high prevalence of classical Kaposi's sarcoma in the Druze of Northern Israel (29). Atzmon et al. (2014) have observed lower cancer rates among Druze versus Arab and Jewish populations in Israel (30).

All the populations included in this study live in the same geographical area, with similar environmental conditions. The four Druze villages included in this study, are located no more than 10-15 Km apart. The water sources supplying all the included populations are of similar nature, with average Iodine levels of 4-6 µg/L. The possible effect of specific goiterogenic foods effecting goiter development in the study groups can also be excluded. A previous study of goiter prevalence in Israeli Ethiopian immigrants found that goiter presence was equally distributed in patients who maintained either Israeli or Ethiopian traditional diets (28). In survey from 2020 of the general Israeli population, no significant differences were found between Arabs – Muslims or Druze and Jewish families in regard to healthy foods consumption (Food Consumption Habits and Attitudes to the Nutrition Labeling Program; Myers-JDC-Brookdale Institute JDC, Jerusalem <https://brookdale.jdc.org.il/en/publication/food-consumption-habits-and-attitudes-to-nutrition-labeling-program/>). In addition to the above mentioned, as a result from the Israeli shopping habits, the majority of the included patient families purchase their basic foods in the same locations – various retail stores located in the area.

The early detection of thyroid goiter is of high importance. An enlargement of goiter can result in symptoms related to tracheal or esophageal compression (dyspnea and/or dysphagia). Early detection and treatment can prevent possible complication such as progressive enlargement or mediastinal extension (tracheal narrowing, superior vena cava syndrome). Cosmetic discomfort resulting from an enlarged goiter - especially in female patients is of no less importance. In contrast to medical therapy, which at best results in partial reduction in goiter volume, surgery offers the possibility of definitive treatment with removal of the goiter (6). Early detection can allow prompt surgery while goiter size is still small. Delayed surgical treatment can result in possible complication such as damage to the recurrent laryngeal nerve or hypocalcemia due to a larger goiter size. Our results can point to the possible benefit of promoting early thyroid screening in the Druze community, especially in women.

We also found a high prevalence of Goiter in the Muslim population (SIR 1.44 CI 1.02-2.00). It should be noted that this group had only 34 (8.7%) patients compared to the other groups included in the study. This low sample size can affect SIR value, and doesn't allow a clear conclusion. These findings are of interest and can open a new possibility for future investigations.

Conclusion

Our results demonstrate a high prevalence of Goiter in the Druze population compared to other ethnic groups in northern Israel. The possible benefit of promoting early thyroid screening in the Druze community, especially in women should be considered. Further studies of possible genetic factors are warranted. A larger study of goiter prevalence in the Israeli Muslims should also be considered.

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