Application of generalized linear mixed model with asymmetric random effects in determination of effective factors related to visible goiter with the health survey data

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Abstract: To evaluate the visible goiter prevalence and its risk factors in Iran using the generalized linear mixed model as the only visible complication of iodine deficiency. **Material and Method**: We used the data of 53633 people who were selected in the national health survey. In order to study risk factors of visible goiter simultaneously, we used a generalized linear mixed model with asymmetric random effects. **Result:** The prevalence of goiter and visible goiter was 32.1% and 4.5%, respectively. The prevalence of goiter and visible goiter was different in rural and urban and also in the age and sex categories, (all p-values<0.001). The odds of the visible goiter in women was 2.29 times higher than men (credible interval 95%=(2.09,2.50)). The adjusted odds ratio of the visible goiter was 1.39 times higher in rural people compared to urban people (credible interval 95%= (1.28,1.50)). The prevalene of visible goiter was highest in 13 to 18 years old people (6%). **Conclusion:** More attention is needed on the nutrition of women, 13 to 18 years old people, and rural resident to prevent the visible goiter

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1.Introduction

An iodine deficiency disorder is one the more important health and nutritional problem. About 2 billion people worldwide are affected by a continual deficiency of crucial minerals and vitamins(1-3). Among theem, 180 million people have goiter with different severity depending on their living geographic location(4). Other iodine deficiency complications varies in different age stages. In fetus causes abortion,still birth, congenital abnormalities, and increase in birth mortality. Also, iodine deficiency causes psychomotor and mental disorders, hypothyroidism (5), and neurological cretinism myxedematous, spastic diplegia (6), defness**,** mental retardation in childhood. In adolescents also hypothyroidism psychological and physical retardation and mental retardation (7-8). However, in most cases, people who live in regions with iodine deficiency, the only apparent complication is goiter(8). The,ost prevalent of iodine deficiency in children was estimated in Eastern Mediterranean (46.6%), European (44.2%), and African (40.4%) regions(1). There have been several studies related to the iodine deficiency in Iran among them the first one carried by the National Iranian Nutrition Institution in 1969 (9-10). Since most iodine deficiency disorders can be prevented with a healthy nutrition having enough iodine supplements, the IDD committee in Iran was formed in 1989. In this year, supply and distribution of iodine salt was chosen as the main strategic solution to the iodine deficiency disorder (11). On of the health survey research in Iran has been quantifying the goiter incidence in the country. Cluster sampling was used to select the participants. Therefore, design effect is anticipated in this sampling and regression analysis takeing this into consideration will result in different regression coefficient and inference compared to the classic models (12-14). Random effects models can take this desing effect into account. However the normality assumption of random effect in these models can affect the robustness of their estimations(15). Using a skewed random effect can be consider as a solution. In this study we used such different analytical aspects to evaluate the effect of different variables on visible goiter.

2.Material and Methods

The first comprehensive health survey research in Iran was conducted by the ministry of health of Iran in 1990 for the purpose of evaluating problems related to the health and remedy of Iranian people(16). The second health survey in Iran was conducted in 1999 by the ministry of health. One of the goals of this comprehensive survey was to determine the prevalence of the goiter disease. The details of sampling method and examinations are reported in another paper (17). Here we present a summary of it. A cluster sampling was used in this survey and it covers all Iranian 2 years old or above

with each clusters containing 8 households. The ratio of sampling to population was 1 to 1000. According to the Iranian census in 1996, the total numbers of households in Iran was 12,359,295 (7,948,925 urban and 4,410,370 rural). Therefore, in this study, considering the country's population growth, 1,097 clusters from urban areas (8,776 households), and 590 clusters from rural areas (4,719 households) were chosen. The sample size in this study was 56,196 people with the information related to thyroid were on 53,633 (95.4%) people. Thyroid grades were evaluated by a physician. For this purpose, the physician stands behind the patient and with both hands exams the region under Adam's apple and up to the supra sterna notch. Based on this overall examination, the thyroid status was categorized in the following five grades.

Grade Zero – Non visible, Non palpable
Grade 1A – Non visible, Palpable
Grade 1B – Visible only when head tilts, Palpable
Grade 2– Thyroid gland is visible in normal position
Grade 3–Thyroid gland is visible from distant (6 meters)

Variables related to goiter that has been investigated in this study are age categorized in four groups of 2-6 years, 7-12 years, 13-18 years, and above 18 years. Also, variables sex and residential place (rural, urban) have been considered. People with goiter grade 1A or above are generally designated as havening goiter and people with goiter grade 2 or above are named as having visible goiter. We used logistic regression with skewed random effects to investigate relationship between qualitative and quantitative variables and to compute odds ratios (OR) when necessary. All statistical analyses were performed in the R statistical software (version 3.0).

3.Results

Table 1 indicates the thyroid status based on age, gender, and residential. According to this table, 36,422 (67.9%) people are with no goiter disease (i.e. grade zero). As it can be seen in this table, the goiter frequencies are different at different age groups (p-value < .001). Also, when considering each goiter grades, difference between rural and urban as well as the difference between male and female of thyroid prevalence is significant (p-value < .001). Table 2 shows, thyroid status according to age and gender. As indicated in this table, the visible goiter prevalence is statistically higher in females than males (6.1% vs. 2.7%; p-value < .001). Furthermore, the significant differences exist for visible goiter prevalence in different age groups, except 2-6 years old people (p-value < .01). However, the difference between male to female visible goiter prevalence increases by age (see Table 2). This information also indicates that the visible goiter prevalence increases substantially at around adolescence ages for both genders and decreases afterward. The visible goiter prevalence for the males decreases from 4.4% for age 13-18 years to 2.4% for age above 18 and for the females from 7.4% to 7.1% for the same age groups. Table 3 shows, thyroid status according to age and residential. As shown in this table, the visible goiter prevalence is statistically higher in rural than in urban areas (5.4% vs. 4%; p-value<.001). Furthermore, the significant differences between residential areas exist for visible goiter prevalence in different age groups, except 2-6 years old people (p-value < .01). In general there have been 17, 211 (32.1%) people with goiter and 2,426 (4.5%) people with visible goiter. The prevalence of goiter and visible goiter is demonstrated in Figure 1 and Figure 2, respectively.

Table 4 contains results of fitting a multiple logistic regression to the goiter data. For the purpose of logistic regression analysis, the goiter status has been classified in two different groups, namely with visible goiter (class 1) and without visible goiter (class 0). In which the 2-6 years age group, gender and urban residential area are supposed as -baseline groups. Area indicate rural residential area and sex indicate female. Based on this model, it can be shown that the prevalence of visible goiter in 2-6 years age group is 0.6%. Comparison with this group, there is a substantially increase in prevalence of goiter in other age groups especially around adolescence ages. This is so that in age group 13-18 years the odds of having a visible goiter is a bout 10 times more than age group 2-6 years old with a 95% credible interval between 8.1 and 14. Therefore, this increase in age increases the probability of goiter for the rural female from 0.011 to 0.10 and for the urban females from 0.008 to 0.07. For the case of rural males, this probability increases by age from 0.005 to 0.047 and for the urban males from 0.003 to 0.032. In addition, according to these findings, the odds of having a visible goiter in females is about 2.3 of the same odds for males (95% CI 2.1-2.5). This pattern is so that for the rural residents' with ages between 13 to 18 years which has the highest prevalence, the probability of goiter increases from 0.047 for male to 0.10 for females. Also, for the urban residents' with ages between 13 to 18 years which again has the highest prevalence, the probability of goiter increases from 0.032 for male to 0.07 for females. On the other hand, our results indicates that the odds of visible goiter in rural areas is 1.4 times the same odds for the urban areas (95% CI 1.3 – 1.5).

Table 1. The prevalence of goiter by demographic characteristics of population.

					Prevalence of kinds of goiter			
Var			**No**	Grade 0	Grade 1A	Grade 1B	Grade 2	Grade 3
				No (%)	No (%)	No (%)	No (%)	No (%)
Sex	**M**		24,936	17996(72.2%)	4331(17.4%)	1925(7.7%)	590(2.4%)	94(0.4%)
	F		28,697	18426(64.2%)	5424(18.9%)	3105(10.8%)	1352(4.7%)	390(1.4%)
Area	**Urban**		33,651	23488(69.8%)	5911(17.6%)	2912(8.7%)	1063(3.2%)	277(0.8%)
	Rural		19,982	12934(64.7%)	3844(19.2%)	2118(10.6%)	879(4.4%)	207(1.0%)
Age (yr)	**2-6**		5,676	4962(87.4%)	496(8.7%)	182(3.2%)	33(0.6%)	3(0.1%)
	7-12		9,649	6765(70.1%)	1673(17.3%)	829(8.6%)	327(3.4%)	55(0.6%)
	13-18		9,083	5538(61.0%)	1867(20.6%)	1136(12.5%)	457(5.0%)	85(0.9%)
	18+		29,225	19157(65.6%)	5719(19.6%)	2883(9.9%)	1125(3.8%)	341(1.2%)
	Total		53,633	36422(67.9%)	9755(18.2%)	5030(9.4%)	1942(3.6%)	484(0.9%)

Table 2. The prevalence of all types of goiter in each gender by age groups

						Type of goiter		
Age (yr)	**Sex**	**No**		**Grade 0**	**Having goiter**	**Grade 1A**	**Grade 1B**	Grade 2+
								(Visible Goiter)
				No (%)	No (%)	No (%)	No (%)	No (%)
2-6	M	2,974		2572(86.5%)	402(13.5%)	271(9.1%)	106(3.6%)	25(0.8%)
	F	2,702		2390(88.5%)	312(11.5%)	225(8.3%)	76(2.8%)	11(0.4%)
6-12	M	4,894		3476(71.0%)	1418(29.0%)	859(17.6%)	391(8.0%)	168(3.4%)
	F	4,755		3289(69.2%)	1466(30.8%)	814(17.1%)	438(9.2%)	214(4.5%)
13-18	M	4,282		2680(62.6%)	1602(37.4%)	900(21.0%)	514(12.0%)	188(4.4%)
	F	4,801		2858(59.5%)	1943(40.5%)	967(20.1%)	622(13.0%)	354(7.4%)
18+	M	12,786		9268(72.5%)	3518(27.5%)	2301(18.0%)	914(7.1%)	303(2.4%)
	F	16,439		9889(60.2%)	6550(39.8%)	3418(20.8%)	1969(12.0%)	1163(7.1%)

Table 3. The prevalence of all types of goiter in area of residency by age groups.

					Prevalence of kinds of goiter		
Age (yr)	**Area**	**No**	**Grade 0**	**Having goiter**	**Grade 1A**	**Grade 1B**	Grade 2+
							(Visible Goiter)
			No (%)	No (%)	No (%)	No (%)	No (%)
2-6	Urban	3,230	2891(89.5%)	339(10.5%)	229(7.1%)	93(2.9%)	17(0.5%)
	Rural	2,446	2071(84.7%)	375(15.3%)	267(10.9%)	89(3.6%)	19(0.8%)
6-12	Urban	5,777	4208(72.8%)	1569(27.2%)	939(16.3%)	437(7.6%)	193(3.3%)
	Rural	3,872	2557(66.0%)	1315(34.0%)	734(19.0%)	392(10.1%)	189(4.9%)
13-18	Urban	5,778	3659(63.3%)	2119(36.7%)	1130(19.6%)	681(11.8%)	308(5.3%)
	Rural	3,305	1879(56.9%)	1426(43.1%)	737(22.3%)	455(13.8%)	234(7.1%)
18+	Urban	18,866	12730(67.5%)	6136(32.5%)	3613(19.2%)	1701(9.0%)	822(4.4%)
	Rural	10,359	6427(62.0%)	3932(38.0%)	2106(20.3%)	1182(11.4%)	644(6.2%)

Table 4 simultaneous effect of different factors on the visible goiter

parameter	Prevalence	OR	95% CI	
			Lower	Upper
Age(yr)				
2-6*	0.60%	1		
12-Jul	4%	6.46	4.58	9.1
13-18	6%	9.94	7.08	13.95
18+	5%	8.27	5.94	11.53
Area (Rural)‡	5.40%	1.39	1.28	1.5
Sex (female)‡	6.10%	2.29	2.09	2.51

*Baseline group
‡Baseline group is urban and male
95% CI: Credible Interval 95%

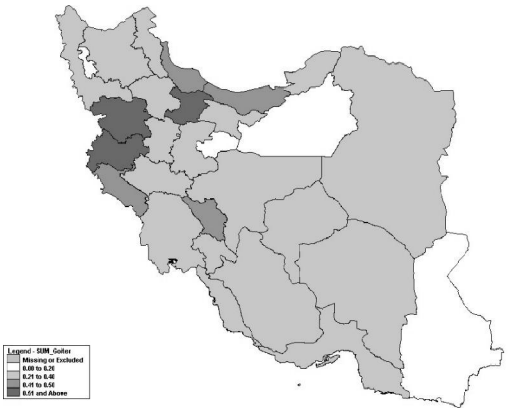

Figure 1. The prevalence of goiter in different province of Iran

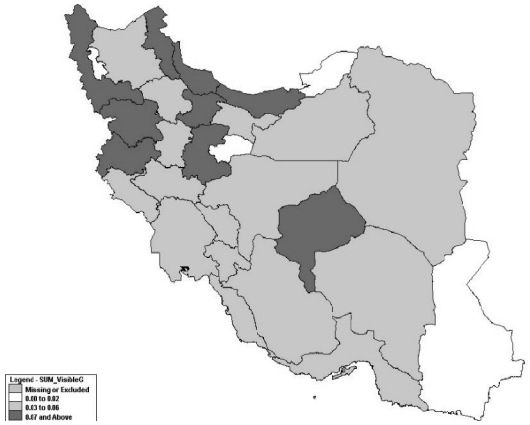

Figure 2. The prevalence of visible goiter in different province of Iran study in Saudi Arabia confirmed such founding (20). In other study in Kashan, Iran province in 1996, the researchers finding was quite similar(21).

Discussion

We have seen in this research that the visible goiter disease has a significant relationship with some variables such as age, gender, and location. This has been confirmed by the other similar researches one of which is the study performed by zali (16). Also, in this research we found that the visible goiter prevalence increases substantially around adolescence ages which again has been found and confirmed in other similar research investigations(18). In addition, the finding in our present research indicates that females have a higher chance for goiter than males.

In one study conducted in Tehran in 1997 specifically on young people, goiter prevalence was found to be higher in girls than in boys(19).

Again, in a study conducted in India in 1994, prevalence of goiter was higher in girls than in boys (22). The effect of iron deficiency on goiter is another issue that has been fully investigated by others (23-24). However, it should be noted that in some studies there has been found no differences among gender (25-26)Perhaps, the main discrepancy between theses studies and ours is the fact that the focus of the latter studies has been on only age groups 8-10 years old. In fact, as indicated earlier, in our study there was no such clear difference between male and female age 2-9 years. In conclusion, in our study and most other similar studies, the goiter prevalence was higher in females. This could be explained by the effect of the sexual hormonal, as also indicated in Razavizadeh, et al 1999(21) . In this study, we found a higher prevalence of visible goiter in rural than in urban areas. In a study conducted in a brackish ground Kashan, Iran(27), also similar results were found. However, in some other studies there was found no difference between goiter prevalence in urban and rural residences(23). As compared with the findings in the Iranian health survey in 1990(16), one can see that the goiter prevalence has increased from 29.4% to 32.1%. On the contrary, the visible goiter prevalence has declined from 5.7% to 4.5%. This is in line with

several study show that there is a decreasing rate in iodine deficiency and goiter in the world and Iran(4, 10, 28-32) This reduction in visible goiter might be partly due to the IDD committee which was formed in 1989 when distribution of the iodine salt has been started. But the overall goiter increases from 1990 to 1999 might be from the fact that there has been a more precise physical examination in the latter survey. Recently, there have been several other studies related to goiter prevalence in Iran. In fact, they used some more precise ways of determining goiter presence such as T3, T4, TSH measurements. However, these studies have been mostly concentrated only on the young people. Our present study does not have this limitation, and uses a much larger sample size and so capable of generalization of the results. Finally, we used the logistic regression with skewed random intercept statistical methodology which has been proven to be much more suitable and robust as compared to the other methods and can consider the correlation in clusters sufficiently.

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