Hypertension and subclinical hypothyroidism : a cross-sectional survey based on population in Gansu Province

Qianqian Liu
First Hospital of Lanzhou University
Xingyu Chang
First Hospital of Lanzhou University
Yaqi Wang
First Hospital of Lanzhou University
Songbo Fu (fusb@lzu.edu.cn)
First Hospital of Lanzhou University
Xulei Tang
First Hospital of Lanzhou University
Gaojing Jing
First Hospital of Lanzhou University
Qianglong Niu
First Hospital of Lanzhou University
Weiping Teng
The First Affiliated Hospital of China Medical University

Research Article

Keywords: Hypertension, subclinical hypothyroidism, risk factors

Posted Date: November 18th, 2022

DOI: https://doi.org/10.21203/rs.3.rs-2274033/v1

Abstract

Purpose: To investigate the prevalence and related influencing factors of subclinical hypothyroidism (SCH) in patients with hypertension (HTN).

Patients and Methods: The 2,818 adult residents in Gansu Province were selected by the multi-stage stratified cluster random sampling method, and the prevalence of standardization was calculated using the direct mapping method. General data and related biochemical indexes were recorded to analyze the prevalence of HTN and SCH. The HTN population was divided into grade 1 HTN, grade 2 HTN and grade 3 HTN groups. The χ^2 test was used to analyze the differences in the prevalence of HTN and SCH in age, sex and thyroid antibody levels. The Logistic regression analysis model was used to analyze the risk factors for SCH in the HTN population.

Results:A total of 2,818 study subjects were included, with 591 SCH patients and 604 HTN patients. The prevalence of SCH was higher in HTN populations under 60 years than in normotensive population (28.95% vs 17.58%, χ^2=21.180, P < 0.05).In this study, we found that whether considering the physiological increase of TSH level in the elderly(using higher TSH cut-offs for people over 65 years) has a greater impact on the prevalence of SCH in the elderly population. We compared and analyzed the two situations. Excluding the physiological increase of TSH levels in the elderly, the prevalence of SCH in the HTN population is higher than that in the normal population (χ^2=40.039, P< 0.05).Considering this effect (using higher TSH cut-offs for people over 65 years), the prevalence of SCH decreased significantly (from 28.00% to 4.00% in normal blood pressure population, from 28.89% to 6.67% in high-normal blood pressure population, and from 34.73% to 7.19% in HTN population, all P 0.05).The prevalence of SCH was higher in the HTN population, whether or not considering the effect of age on TSH, than in the normal blood pressure population (24.34% vs 17.28%, χ^2=11.813;31.95% vs 17.86%, χ^2 =40.039,both P<0.05). Moreover, the prevalence of SCH between normal blood pressure,high-normal blood pressure and HTN population were significantly different(P < 0.05). In the HTN population, the DBP, TC, TSH, blood phosphorus, TPOAb, and TgAb levels were higher in the SCH group than in the normal group P < 0.05). The TPOAb and TgAb levels were higher in women in the SCH population than in men (P < 0.05).Considering the physiological increase of TSH levels in the elderly, the prevalence of SCH in the total HTN population and grade 2 population with SCH was higher than in thyroid antibody negative patients 35.90% vs 22.62%, P<0.05).The Logistic regression analysis showed that the risk factors for SCH in the HTN population were FPG, TG, LDL-C, TPOAb, and TgAb, and the protective factor was heart rate (P < 0.05).

Conclusion: The prevalence of SCH in the HTN population was relatively high and was significant in female population. The authenticity of SCH in the elderly population caused by the physiological increase of age-related TSH needs to attract more attention. The HTN population should be careful to monitor the correlation of their own glucose metabolism levels and TSH.

Introduction

With the development of social economy and the change of people's lifestyle, the risk of hypertension (HTN) is increasing. At present, the prevalence rate of HTN in China could reach as high as 27.9%, which has become one of the high-risk chronic diseases that seriously affect the health of residents.[1] Subclinical hypothyroidism (SCH) patients usually lack obvious clinical symptoms and signs, so it is easy to be ignored and develop into clinical hypothyroidism and seriously endangers the health of patients .[2~4] The national epidemiological survey showed that the prevalence rate of hypothyroidism in adults in China was 17.8%, among which SCH was 16.7% and clinical hypothyroidism was 1.1% ,[5] so it is particularly important to pay attention to the prevention and treatment of SCH. Studies have shown that elevated blood pressure is positively correlated with the occurrence of thyroid-related diseases,[6] but there are relatively few studies on the prevalence of SCH in HTN population. This study selected residents in Gansu Province as the object to explore the relationship between blood pressure level and SCH, and to provide reference ideas for the clinical prevention and treatment of SCH in HTN population.

Material And Methods

Research object

Selection method: This study is a cross-sectional observational study designed to evaluate the prevalence of subclinical hypothyroidism and its associated factors in hypertensive patients (confirmed cases already on antihypertensive therapy). A multi-stage stratified cluster random sampling method was used in Gansu Province. From September 4, 2016 to February 1, 2017, adult Han residents living in Lanzhou, Longnan, Dingxi, Baiyin and Linxia for more than 5 years were randomly selected. Following the procedure of ' registration first and mobilization later ', the registered population at each site should be more than twice the size of the sample to meet the number of samples and the requirements of gender and age structure,and to prevent voluntary entry into the investigation queue by persons outside the site. A total of 2818 subjects were included, including 1445 males and 1373 females. The age range was 18–87 years, and the average age was 42.76 ± 15.00 years. Exclusion criteria: (1)Those who meet the diagnosis of hyperthyroidism, subclinical hyperthyroidism, hypothyroidism or are receiving treatment for the above diseases. (2)Patients with severe heart, liver, renal insufficiency, severe anemia or malignant tumor. (3)Patients who had no obvious symptoms and the results were at the critical value were followed up for 2–3 months and then measured again as normal. (4)Patients who are taking medicine affecting thyroid function test, such as glucocorticoids, metoclopramide, propranolol, etc. (5)pregnant women or lactating women. (6)People with irregular use of antihypertensive drugs and unstable blood pressure

Method

Clinical data

Under the guidance of professionals, the participants filled out the survey registration form and accurately recorded gender, age, height, weight, body mass index (BMI), waist circumference, heart rate, systolic blood pressure (SBP), diastolic blood pressure (DBP), family history of diabetes, history of hypertension,

history of thyroid disease, and other general conditions.

We obtained ethical approval and a letter of cooperation from the Medical Ethics Research Committee of the First Affiliated Hospital of China Medical University (AF-SOP-07-1.0-01), which was conducted in accordance with the Declaration of Helsinki.

Biochemical index

The blood lipid-related indexes: total cholesterol (TC, mmol/L), triglyceride (TG, mmol/L), high-density lipoprotein cholesterol (HDL-C, mmol/L), and low-density lipoprotein cholesterol (LDL-C, mmol/L); uric acid (UA, mmol/L),aspartate aminotransferase (AST), alanine aminotransferase (ALT), blood calcium and serum phosphate(mmol/L)using test kit and biochemical analyzer (BS-180, Mindray company). Fasting plasma glucose (FPG, mmol/L) and 2 h blood glucose after OGTT load (2h PG, mmol/L) were determined by glucose oxidase method using test kit and biochemical analyzer (BS-180, Mindray company). Glycosylated hemoglobin(HbA1c, %) using BioRad reagent, measured by VARIANT II (BioRad Company).Thyroid-stimulating hormone (TSH, mIU/L), Free thyroxine (FT4, pmol/L) anti-thyroid peroxidase antibody (TPOAb, 0 ~ 34IU/L), and anti-thyroid globulin antibody (TgAb, IU/L) using ICMA (Roche Company). Urinary iodine (UIC, g / L) was determined by inductively coupled plasma mass spectrometer (7700x, Agilent, USA).

Diagnostic criteria and grouping of blood pressure

According to the classification and definition of blood pressure levels in ' Guidelines for the Prevention and Treatment of Hypertension in China (revised 2018) '[1] : (1) Normal blood pressure : SBP < 120 mmHg and DBP < 80 mmHg ; (2) normal high values : 120 mmHg ≤ SBP ≤ 139 mmHg and / or 80 mmHg ≤ DBP ≤ 89 mmHg ; (3) Hypertension : SBP ≥ 140mmHg and / or DBP ≥ 90mmHg ; (4) Simple systolic hypertension : SBP ≥ 140 mmHg and DBP < 90 mmHg. HTN was divided into grade 1 hypertension (mild) : 140 mmHg ≤ SBP ≤ 159 mmHg and / or 90 mmHg ≤ DBP ≤ 99 mmHg ; grade 2 hypertension (moderate) : 160 mmHg ≤ SBP ≤ 179 mmHg and / or 100 mmHg ≤ DBP ≤ 109 mmHg ; grade 3 hypertension (severe) : SBP ≥ 180 mmHg and / or DBP ≥ 110 mmHg. When the SBP and DBP grades belong to different levels, the higher grade shall prevail.

Subclinical hypothyroidism

In reference to the Guidelines for the Diagnosis and Treatment of Adult Hypothyroidism and An Age-Specific Serum Thyrotropin Reference Range for the Diagnosis of Thyroid Diseases in Older Adults: A Cross-Sectional Survey in China,[7,8] the criteria are as follows: normal free thyroxine (FT4:9.00 ~ 22.00 pmol/L) and free triiodothyronine (FT3: 3.1–6.8 pmol/L) levels and elevated thyroid-stimulating hormone : Consider the impact of age on TSH: TSH > 4.20 mIU/L(age ≤ 65),TSH > 8.86 mIU/L (age 65). Do not consider the impact of age on TSH: TSH > 4.20 mIU/L.

Statistical method

SPSS software (version 26.0) was used for statistical analyses. Normal distribution measurement data are expressed as (x ± s). Two independent sample t-tests were used for comparisons between the two groups. Count data were described by frequency. The χ2 test was used to analyse the differences between HTN and SCH populations(with age and gender stratification) and the differences in prevalence between the two groups. A logistic regression analysis model was used to analyse the possible risk factors for HTN, with a test level of α = 0.05. Non-normal distribution data were expressed as median (median, M), 25th, and 75th percentiles (P_{25} and P_{75}, respectively). The Mann-Whitney U test was used for comparisons between the two groups. All of the comparison results were statistically significant ($P < 0.05$).

Results

Comparison of general data between SCH group and Normal group in hypertensive population

There are 604 subjects with hypertension in 2818.And the 604 subjects with hypertension were divided into normal and SCH groups. Analysis of the general data of 604 patients with hypertension revealed that the levels of DBP,TC,TSH,Serum phosphate, TPOAb and TgAb in the SCH group were higher than those in the normal group (all $P < 0.05$). The levels of TSH, TPOAb and TgAb in female were higher than those in male in the normal group, and the level of TPOAb and TgAb in female was higher than that in male in SCH group (all $P < 0.05$). The corresponding results are shown in Table 1a and Table 1b.

Table 1a

Comparison of general data between the SCH and Normal groups in hypertensive populations

Characteristics	Total n=604			
	Normal	SCH	t/z	*P*
	n=457,75.66%	n=147 24.34%		
Age	55.35±15.10	53.66±11.42	1.440	0.151
BMI/ kg/m^2	25.09±3.36	25.10±3.20	-0.024	0.980
SBP/mmHg	152.27±16.84	153.80±15.65	-0.971	0.332
DBP/mmHg	89.90±12.33	92.62±11.39	-2.371	0.018
Heartrate/bpm	82.68±12.52	79.54±11.74	-2.684	0.007
FPG/(mmol/L)	6.07±2.14	6.06±2.01	0.096	0.923
2hPG/(mmol/L)	8.75±4.85	8.03±4.10	1.779	0.076
TG/(mmol/L)	1.86±1.35	1.94±1.84	-0.59	0.555
TC/(mmol/L)	4.70±0.96	4.95±0.92	-2.792	0.005
LDL-C/(mmol/L)	2.81±0.76	2.90±0.68	-1.333	0.183
HDL-C/(mmol/L)	1.49±0.40	1.52±0.35	-0.604	0.546
TSH/(mIU/L)	2.74±1. 38	7.05±3.43	-14.846	0.001
ALT/ U/L	25.72±22.73	27.02±17.77	-0.636	0.525
AST/(U/L)	30.25±19.67	32.16±13.50	-1.095	0.274
Ca/ mmol/L	2.20±0.11	2.21±0. 10	-0.761	0.447
Serum phosphate/ mmol/L	0.99±0.16	1.02±0. 17	-2.435	0.015
25-OH-D/(ng/ml)	13.94±6.24	14.18±6.77	-0.392	0.695
HbA1c/%	5.85±1.25	5.63±0.99	1.925	0.055
UA M P25,P75)/(μmol/L)	277.00 217.00,338.50	247.00 197.00 314.00	-2.464	0.014
TPOAb M P25,P75)/(IU/ml)	9.70 7.30,14.42	11.94 8.07,16.83	2.985	0.003
TgAb M(P25,P75)/(IU/ml)	11.39 10.00 18.08)	15.48 10.00,23.27	3.681	0.001
UIC M(P25,P75)/(μg/L)	221.40(156.65,309.15	206.70(148.60,296.70)	-0.978	0.328

Table 1b

Comparison of thyroid-related indicators in SCH and Normal group among hypertensive population

Characteristics	**Total(n = 604)**							
	Normal group				**SCH group**			
	Male(n = 253)	**Female(n = 204)**	**t/z**	**P**	**Male, n = 67**	**Female, n = 80**	**t/z**	***P***
TSH (mIU/L)	2.53 ± 1.26	3.01 ± 1.46	-3.722	0.001	6.90 ± 2.99	7.18 ± 3.78	-0.483	0.63
TPOAb	9.38	11.21 (7.45,16.51)	2.568	0.01	9.59	13.36	3.512	0.001
M(P25,P75)/(IU/L)	(7.26, 12.97)				(7.54, 14.25)	(9.95,18.94)		
TgAb	10.55	13.3	3.587	0.001	12.2	17.3	3.443	0.001
M(P25,P75)/(IU/L)	(10.00,15.91)	(10.00,22.77)			(10.00,18.05)	(12.12,64.96)		

Comparison of SCH prevalence in HTN population

This study included 2818 participants in the following cohorts: Normal blood pressure (1002 individuals),High-normal blood pressure (1212 individuals) and HTN (604 individuals). This study also included 591 patients with SCH (249 male, 342 female). The prevalence of SCH in the HTN population was 24.34% (147/604). Furthermore, the prevalence of SCH in female was higher than that in male in normal blood pressure,high-normal blood pressure and HTN populations(20.28% vs 13.18%,28.32% vs 18.00%,28.17% vs 20.94%, all $P < 0.05$), as shown in Table 2.

Table 2
Comparison of SCH prevalence in HTN population

	Male		Female		P^*	χ^2	Total	
	n	n-SCH(%)	n	n-SCH(%)			n(%)	n-SCH(%)
Normal blood pressure	425	56(13.18)	577	117(20.28)	0.003	8.639	1002(35.56)	173(17.27)
High-normal blood pressure	700	126(18.00)	512	145(28.32)	0.001	18.143	1212(43.01)	271(22.36)
Hypertension	320	67(20.94)	284	80(28.17)	0.039	4.273	604(21.43)	147(24.34)
Grade 1 hypertension	202	38(18.81)	168	46(27.38)	0.05	3.838	370(13.13)	84(22.70)
Grade 2 hypertension	87	22(25.29)	81	22(27.16)	0.783	0.076	168(5.96)	44(26.19)
Grade 3 hypertension	31	7(22.58)	35	12(34.29)	0.295	1.099	66(2.34)	19(27.54)
Isolated systolic hypertension	86	14(16.28)	146	30(20.55)	0.423	0.642	232(8.23)	44(18.97)
$P^{\#}$	-	0.016	-	0.003	-		-	0.001
χ^2	-	8.271	-	11.417			-	13.842
Total	1445	249(17.23)	1373	342(24.91)	0.001	25.036	2818(100)	591(20.97)

n: Total number of subjects; n-SCH Number of patients with subclinical hypothyroidism;P^* Comparison between male and female patients with SCH; $P\#$ Comparison between normal blood pressure ,high-normal blood pressure and hypertension patients with SCH

Distribution of HTN and SCH patients in different age groups

The prevalence of SCH in the HTN population under the age of 60 was higher than that in the normal blood pressure population (28.95% vs 17.58%, $\chi^2 = 21.180$, $P < 0.05$). When considering the effect of age on TSH, the prevalence of SCH among the total normal blood pressure,high-normal blood pressure and HTN population was significantly different (17.28% vs 22.36% vs 24.34%, $\chi^2 = 13.842$, $P < 0.05$).; when not considering the effect of age on TSH,the prevalence of SCH among the total normal blood pressure,high-normal blood pressure and HTN population was also significantly different (17.86% vs 24.01% vs 31.95%, $\chi^2 = 39.883$, $P < 0.05$). Regardless of whether the effect of age on TSH was considered, the prevalence of SCH in the high normal blood pressure population was higher than that in the normal blood pressure population ($\chi^2 = 8.879$, $\chi^2 = 11.762$, both $P < 0.05$).the prevalence of SCH in the HTN population was higher than that in the normal blood pressure population ($\chi^2 = 11.813$, $\chi^2 = 40.039$, both $P < 0.05$). Among the three HTN subtypes, the prevalence of SCH in the grade 3 hypertension population were higher(28.79%;37.68%). Age-stratified analysis showed that the prevalence of SCH in the HTN population showed an overall upward trend with an increase age(60). In the ≥ 61-year-old population, the prevalence of SCH in both high-normal blood pressure and HTN populations was significantly higher (14.18%^{a} vs 28.37%^{b}, $\chi^2 = 8.468$;16.88%^{a} vs 36.80%^{b}, $\chi^2 = 23.325$, both P 0.05). In the population ≥ 65 years old, the prevalence of SCH in normal blood pressure,high-normal blood pressure and HTN populations was significantly higher compared with considering the effect of age on TSH without considering the effect of age on TSH(4.00%^{a} vs 28.00%^{b},$\chi^2 = 5.357$;6.67%^{a} vs 28.89%^{b}, $\chi^2 = 15.203$; 7.19%^{a} vs 34.73%^{b} ,$\chi^2 = 38.244$; all P 0.05) ,as shown in Table 3.

Table 3

Distribution of hypertension and subclinical hypothyroidism in patients of different ages

Groups	n	Normal blood pressure		High-normal blood pressure		HTN		HTN grade (example, percentage%) and the distribution of SCH patients					
Age								Grade 1 hypertension		Grade 2 hypertension		Grade 3 hypertension	
		n	SCH(n,%)	n	SCH(n,%)	n	SCH(n,%)	n	SCH(n,%)	n	SCH(n,%)	n	SCH(n,%)
18~30	760	415	55(13.25)	302	59(19.54)	43	9(20.93)	35	7(20.00)	8	2(25.00)	0	0
31~40	620	297	50(16.84)	267	49(18.35)	56	9(16.07)	32	0	16	8(50.00)*	8	1(12.50)
41~50	611	166	33(19.88)	325	85(26.15)	120	27(22.50)	78	15(19.23)	26	6(23.08)	16	6(37.50)
51~60	420	89	32(35.16)	177	58(32.77)	154	63(40.91)	101	38(37.62)	38	15(39.47)	15	10(66.67)#
Total	2411	967	170(17.58)	1071	251(23.44)	373	108(28.95)	246	60(24.39)	88	31(35.23)	39	17(43.59)
(18~60)													
≥61[a]	407	35	3(8.57)	141	20(14.18)	231	39(16.88)	124	24(19.35)	80	13(16.25)	27	2(7.41)
≥65[a]	290	25	1(4.00)	90	6(6.67)	167	12(7.19)	86	7(8.14)	61	5(8.20)	20	0
Total[a]	2818	1002	173(17.28)	1212	271(22.36)*	604	147(24.34)*	370	84(22.70)	168	44(26.19)	66	19(28.79)
P	-	0.001		0.001		0.001		0.001		0.015		0.001	
*c*2		29.125		23.026		32.506		23.686		12.386		18.147	
≥61[b]	407	35	9(25.71)	141	40(28.37)	231	85(36.80)	124	44(34.65)	80	32(39.02)	27	9(32.14)
≥65[b]	290	25	7(28.00)	90	26(28.89)	167	58(34.73)	86	27(31.40)	61	24(39.34)	20	7(35.00)
Total[b]	2818	1002	179(17.86)	1212	291(24.01)*	604	193(31.95)*	382	104(27.23)	172	63(36.63)	69	26(37.68)

n: Total number n-SCH Number of patients with SCH % prevalence *P* Comparison of the prevalence of SCH among different ages.*:Comparison between normal blood pressure/high-normal blood pressure and hypertension patients with SCH. Totala: the consideration of the physiological increase of TSH in the elderly, the diagnostic criteria of SCH for people under 65 years old (TSH>4.20 mIU/L, FT3 and FT4 are normal), and different diagnostic criteria for SCH for people over 65 years old (TSH>8.86 mIU/L, FT3 , FT4 normal) the prevalence of SCH. Totalb :the prevalence of SCH based on the same diagnostic criteria for SCH (TSH>4.20 mIU/L, normal FT3 and FT4) for all ages regardless of the effect of age on TSH.

Thyroid antibodies in different populations

In the total population and SCH population, the positive rate of thyroid-associated antibody in female was higher than that of male(all *P* 0.05). In the HTN population, the positive rate of TgAb(+),both TPOAb(+)and TgAb + ,and both negative in female was higher than that of male(*P* 0.05). The positive rate of both TPOAb + and TgAb + and both negative in female was higher than that of male in the SCH combined with HTN population. In the total HTN population, the prevalence of SCH in thyroid antibody-positive patients was significantly higher than that in thyroid antibody-negative patients. In HTN subgroup, especially in grade 2 HTN population, the prevalence of SCH in patients with positive thyroid antibody was also higher than that in patients with negative thyroid antibody (all $P < 0.05$),as shown in Table 4a and Table 4b.

Table 4a
Thyroid antibodies in different populations

Group	Total(2818)		P	χ2	SCH(591)		P	χ2	Hypertension(604)		P	χ2	SCH + hypertension(147)	
Gender	Male	Fe			Male	Fe			Male	Fe			Male	Fe
	(1445)	male			(249)	male			(320)	male			(67)	male
		(1373)				(342)				(284)				(80)
TPOAb(+)	67	149	P 0.001	38.43	21	56	0.005	8.018	20	29	0.075	3.167	5	11
TgAb(+)	57	175	P 0.001	72.185	16	67	P 0.001	20.688	15	35	0.001	11.556	6	14
TPOAb(+)and TgAb +	32	77	P 0.001	21.806	10	31	0.017	5.688	9	12	0.344	0.895	3	5
TPOAb(+)	60	170	P 0.001	63.61	17	61	P 0.001	15.244	17	40	P 0.001	13.547	5	15
or TgAb(+)														
Both negative	1353	1126	P 0.001	89.875	222	250	P 0.001	23.103	294	232	P 0.001	14.338	59	60

Table 4b
Prevalence of SCH at different thyroid antibody levels in the HTN population

	TPOAb(+)		TgAb(+)		TPOAb(+) and TgAb(+)		TPOAb(+) or TgAb(+)		Thyroid antibody (+)		Thyroid antibody (-)		P	χ2
	n	n,%	n	n,%	n	n,%	n	n,%	n	n,%	n	n,%		
Grade 1 hypertension	28	8(28.57)	20	7(35.00)	8	2(25.00)	32	11(34.38)	40	13(32.50)	330	71(21.52)	0.117	2.453
Grade 2 hypertension	15	6(40.00)	23	10(43.48)	10	4(40.00)	18	8(44.44)	28	12(42.86)	140	32(22.86)	0.028	4.828
Grade 3 hypertension	6	2(33.33)	7	3(42.86)	3	2(66.67)	7	1(14.29)	10	3(30.00)	56	16(28.57)	0.927	0.008
Total	49	16(32.65)	50	20(40.00)	21	8(38.10)	57	20(35.09)	78	28(35.90)	526	119(22.62)	0.011	6.499
P:Comparison of the prevalence of SCH in the thyroid antibody-positive and anti-negative population														

Logistic regression analysis of the risk factors for SCH disease in the HTN population

In the HTN populations, with or without SCH as the dependent variable, the independent variables were screened by single-factor analysis, and the independent variables with statistical significance were further evaluated in a multivariate analysis. The results showed that the protective factors for SCH in the HTN population were heartrate ;and the risk factors were TG,LDL-C,TPOAb,TgAb and FPG (all $P < 0.05$),as shown in Table 5.

Table 5
Multivariate Logistic analysis of influencing factors affecting SCH in hypertensive population

	B	SE	Walds	*P* value	OR	95% CI	
						lower limit	upper limit
Heartrate	-0.031	0.009	12.658	< 0.001	0.969	0.953	0.986
TG	0.188	0.088	4.024	0.04	1.198	1.008	1.425
LDL-C	0.557	0.279	3.994	0.046	1.746	1.011	3.016
TgAb	0.001	< 0.001	5.487	0.019	1.001	1	1.002
TPOAb	0.003	0.001	3.881	0.049	1.003	1	1.006
FPG	0.4	0.201	3.976	0.046	1.492	1.007	2.21

Discussion

With the deepening degree of population aging and the rapid development of socioeconomic structure, HTN and SCH have gradually become important factors affecting the health of residents. Studies have pointed out that HTN is closely related to SCH prevalence, but the pathogenesis of HTN resulting in SCH is not yet clear.

The prevalence of SCH in HTN population under 60 years old in Gansu Province was 28.95%, significantly higher than that in normal population (17.58%). However, the prevalence rate of SCH in the whole age group of HTN population was always significantly higher than that in the normal population (24.34% vs 17.28%, χ^2 = 11.813;31.95% vs 17.86%, χ^2 = 40.039,P< 0.05), regardless of whether the TSH level was considered to increase with age physiologically (the SCH diagnostic criteria for people over 65 years old consider TSH > 8.86 mIU/L alone). The diagnostic criteria for SCH in the elderly are still controversial. Professor Biondi et al. have shown that serum TSH levels in elderly patients may exceed the upper limit of the traditional reference range of 4–5 mU / L, which may lead to an overestimation of the true prevalence of subclinical hypothyroidism in people over 70 years of age.[9] Consistent with our study, we found that the prevalence of SCH was higher in people over 65 years of age without considering the effect of age on TSH(normal: 28.00% HTN: 34.73%); the prevalence of SCH in people over 65 years of age decreased significantly when considering the physiological increase of TSH caused by age (normal: 4.00% HTN: 7.19%). Some studies have shown that in the absence of thyroid diseases, the elderly with slightly elevated serum TSH did not increase the incidence of SCH and the risk of death, suggesting that we should update the diagnostic criteria of TSH according to the reference range of TSH in the elderly population in the region.[10] In calculating the prevalence of SCH in the elderly, it is necessary to reconsider the boundary value of TSH to avoid the misdiagnosis of SCH in the population, so that the calculation of the prevalence of SCH is more reasonable, which is helpful for the diagnosis and treatment of clinicians. However, in either case, the prevalence of SCH in Gansu HTN population was lower than that in Chongqing (31.70%) and higher than that in India (8.20%).[11,12] This may be related to the geographical environment, living habits and many other factors in Gansu province, which should be paid attention to. Meanwhile, we found that the grade 3 HTN population had the highest prevalence among the three subtypes of HTN, and HTN population prevalence were higher than the SCH prevalence in the normal population,regardless of considering the effect of age on TSH.

Further gender-stratified analysis of the HTN population found that the prevalence of SCH was always higher in women than in men, consistent with the findings of He et al, who also observed that HTN women were more likely to develop SCH than men.[13] We also found that TPOAb and TgAb levels were higher in SCH group than in normal group, and the prevalence of SCH in thyroid antibody-positive patients was significantly higher than that in thyroid antibody-negative patients in the total HTN population and grade 2 HTN population, while high TPOAb and high TgAb were risk factors for SCH in HTN population. This may be because hypertension by enhancing thyroid inflammation, antiperoxidase antibody cause autoimmune thyroiditis, because thyroid peroxidase has an important role in the synthesis of thyroid hormone, caused by antiperoxidase antibody inhibition, potential thyroid damage caused by antiperoxidase antibody may reduce the effectiveness of thyroid hormone, so that serum TSH concentration compensatory rise, leading to the occurrence of SCH.[14] Meanwhile, we found that thyroid-related antibody levels were significantly higher in women than in men in both normal and SCH populations, suggesting that HTN women need more clinical attention.

Studies have found that high FPG, high TG and high LDL-C are the risk factors for SCH in the HTN population, which may be due to the long-term hypertensive state, hypersympathetic activity, causing insulin resistance, leading to abnormal glycemic and lipid metabolism in the body.[15] People with abnormal glucose and lipid metabolism are more prone to autoimmune responses and thyroid cell destruction. At the same time, leptin levels are high in patients with abnormal glucose and lipid metabolism, which may affect the hypothalamic-pituitary-thyroid axis pathway through Janus activated kinase (JAK) -2 / signaling and transcriptional activation (STAT), so as to stimulate TSH synthesis and affect thyroid function.[9] This finding suggests that HTN patients should be paid attention to thyroid function-related indicators.

Moreover, we found lower heart rate in SCH patients in HTN population. Klein et al also found lower heart rate in SCH patients,[16] and the Logistic regression analysis model also showed that heart rate is a protective factor for SCH in HTN population, probably because HTN is a risk factor for atherosclerosis,[17] and the diffuse atherosclerosis of coronary artery also often lead to lower coronary blood flow reserve, which may lead to dilated myocardial ischemia and perfusion, heart blood supply oxygen, so the heart rate increased.[18] SCH patients often with slower heart rate, cardiac output and systemic vascular resistance increase,[4] so elevated heart rate in HTN patients may prevent SCH.

The prevalence of SCH is high in the HTN population, and studies show that HTN is a risk factor for atherosclerosis, which can affect the blood supply of the thyroid gland, and thus inhibit the thyroid function.[19,20] Other studies have shown that the vast majority of HTN patients have different forms of metabolic disorders, and the metabolic disorders in the body can affect the secretion of TSH, and then affect the occurrence of SCH. The metabolic disorders in HTN patients can also hinder the energy utilization of thyroid follicle cells, resulting in iodine pump not working normally, and the body TSH level reaction increases.[20,21] In addition, HTN is an immune-inflammatory mechanism mediated disease.[22] Increased inflammatory cytokines such as interleukins in patients can inhibit the synthesis of thyroid peroxidase mRNA, thereby inhibiting the synthesis of thyroid hormones.[23] Under the regulation of the hypothalamus-pituitary-thyroid axis, the body TSH level is increased to maintain the normal circulating thyroid hormone level.[24]

Conclusion

In conclusion, the prevalence of SCH is high in the HTN population in Gansu Province, and the further subdivision of SCH severity may provide the next research direction to study the relationship between SCH and HTN. However, there are still some defects in our study. The accuracy of the determination of TSH level at a single time point on the true situation of thyroid function level is worth thinking about, but given the actual situation and ethical requirements, we failed to determine several times, which we need to pay attention to in the future.

Abbreviations

TPOAb = Thyroid peroxidase antibody; TgAb = Thyroglobulin antibody; SBP = Systolic blood pressure; DBP = Diastolic blood pressure; BMI = Body mass index; FPG = Fasting plasma glucose; OGTT 2hPG = Oral glucose tolerance test 2hPG; HbA1c = Glycated hemoglobin; LDL-C= Low-density lipoprotein cholesterol; HDL-C= High-density lipoprotein cholesterol; TG = Triglycerides; TC = Total cholesterol; TSH = Thyroid-stimulating hormone; FT4 = Free thyroxine; FT3 =Free triiodothyronine; UA = Uric acid. UIC=Urinary iodine AST=aspartate aminotransferase; ALT=alanine aminotransferase

Declarations

Ethical Consideration

We obtained ethical approval and a letter of cooperation from the Medical Ethics Research Committee of the First Affiliated Hospital of China Medical University (AF-SOP-07-1.0-01), and our study was conducted in accordance with the Declaration of Helsinki. All of the study participants provided written informed consent and were informed of the confidentiality, purpose, and importance of their information.

Consent for publication

Not applicable

Data availability statement

The data that support the findings of this study are available from the corresponding author.

Competing interests

The authors declare that they have no competing interests

Funding

2020 special project for the central government to guide local science and technology development (innovative platform for improving the ability of prevention and control of frequently-occurring diseases in Gansu Province, China) Gansu Province Endocrine Disease Clinical Medicine Research Center Construction Plan (20JR10FA667); Natural Science Foundation of Gansu Province (20JR10RA681); Lanzhou Science and Technology Development Guiding Plan Project (2019-ZD-38); National Health and Family Planning Commission Public Welfare Industry Scientific Research Project (201402005); The National Key R and D Program "Prevention and Control Research" 2017YFC1310700,2017YFC1310702;Lanzhou University 2021 College Students Innovation and Entrepreneurship (20220060112).

Author contributions

All authors contributed to the study conception and design.The specific division of labor is as follows:

Songbo Fu: contributed to conception, design, data collection and analysis. Critically revised the manuscript.

Qianqian Liu,Xingyu Chang: contributed to the conception, design, data processing, statistical analysis Graphics rendering and drafting the manuscript.

Yaqi Wang: contributed to the data processing, statistical analysis and Graphics rendering.

Xulei Tang, Gaojing Jing, Qianglong Niu,Weiping Teng: contributed to participation in data collection. Critically revised the manuscript.

All authors commented on previous versions of the manuscript. All authors read and approved the final manuscript

Acknowledgments

We would like to thank everyone who participated in this study and helped collect data. And to thank all the anonymous participants for responding to our questions.

References

1. Chinese Guidelines for the Prevention and Treatment of Hypertension. (Revised Edition, 2018). The Chinese Journal of Cardiovascular Medicine,2019,24(01):24–56.DOI: 10. 3969 /j. issn. 1007–5410. 2019. 01. 002.
2. O'Grady MJ, Cody D. Subclinical hypothyroidism in childhood. Arch Dis Child. 2011;96(3):280–4. doi:10.1136/adc.2009.181800.
3. Razvi S, Pearce SH. Subclinical hypothyroidism and cardiovascular disease-reply. Arch Intern Med. 2012;172(19):1523–4. doi:10.1001/2013.jamainternmed.597.
4. Oner FA, Yurdakul S, Oner E, Uzum AK, Erguney M. Evaluation of the effect of L-thyroxin therapy on cardiac functions by using novel tissue Doppler-derived indices in patients with subclinical hypothyroidism. Acta Cardiol. 2011;66(1):47–55. doi:10.1080/ac.66.1.2064966.
5. Shan Z, Chen L, Lian X, et al. Iodine Status and Prevalence of Thyroid Disorders After Introduction of Mandatory Universal Salt Iodization for 16 Years in China: A Cross-Sectional Study in 10 Cities. Thyroid. 2016;26(8):1125–30. doi:10.1089/thy.2015.0613.
6. Polat Canbolat I, Belen E, Bayyigit A, Helvaci A, Kilickesmez K. Evaluation of Daily Blood Pressure Alteration in Subclinical Hypothyroidism. Acta Cardiol Sin. 2017 Sep;33(5):489–94. doi:10.6515/acs20170220b. PMID: 28959101; PMCID: PMC5611345.

7. Guidelines for the diagnosis and treatment of adult hypothyroidism[J].Chinese Journal of Endocrinology and Metabolism,2017,33(02):167–180.DOI:10.3760/cma. j. issn. 1000–6699. 2017. 02. 018.
8. Zhai X, Zhang L, Chen L, et al. An Age-Specific Serum Thyrotropin Reference Range for the Diagnosis of Thyroid Diseases in Older Adults: A Cross-Sectional Survey in China. Thyroid. 2018;28(12):1571–9. doi:10.1089/thy.2017.0715.
9. Biondi B, Kahaly GJ, Robertson RP. Thyroid Dysfunction and Diabetes Mellitus: Two Closely Associated Disorders. Endocr Rev. 2019;40(3):789–824. doi:10.1210/er.2018-00163.
10. Gussekloo J, van Exel E, de Craen AJ, Meinders AE, Frölich M, Westendorp RG. Thyroid status, disability and cognitive function, and survival in old age. JAMA. 2004;292(21):2591–9. doi:10.1001/jama.292.21.2591.
11. Cai P, Peng Y, Chen Y, Wang Y, Wang X. Blood pressure characteristics of subclinical hypothyroidism: an observation study combined with office blood pressure and 24-h ambulatory blood pressure. J Hypertens. 2021;39(3):453–60. doi:10.1097/HJH.0000000000002655.
12. Talwalkar P, Deshmukh V, Bhole M. Prevalence of hypothyroidism in patients with type 2 diabetes mellitus and hypertension in India: a cross-sectional observational study. Diabetes Metab Syndr Obes. 2019;12:369–76. doi:10.2147/DMSO.S181470. Published 2019 Mar 20.
13. He J, Lai Y, Yang J, et al. The Relationship Between Thyroid Function and Metabolic Syndrome and Its Components: A Cross-Sectional Study in a Chinese Population. Front Endocrinol (Lausanne). 2021;12:661160. doi:10.3389/fendo.2021.661160. Published 2021 Mar 31.
14. Shimizu Y, Kawashiri SY, Noguchi Y, Nagata Y, Maeda T, Hayashida N. Anti-thyroid peroxidase antibody and subclinical hypothyroidism in relation to hypertension and thyroid cysts. PLoS ONE. 2020;15(10):e0240198. doi:10.1371/journal.pone.0240198. Published 2020 Oct 2.
15. Jiawang Yu, Xiulian W, Ren Z, Wei D, Wei S. Wang Bangning. Relationship between resting heart rate and family self-measured blood pressure variation and glucose and lipid metabolism disorders in hypertensive patients [J]. Chin J Clin Health Care. 2017;20(01):7–10.
16. Klein I, Ojamaa K. Thyroid hormone and the cardiovascular system. N Engl J Med. 2001;344(7):501–9. doi:10.1056/NEJM200102153440707.
17. Baycan S, Erdogan D, Caliskan M, et al. Coronary flow reserve is impaired in subclinical hypothyroidism. Clin Cardiol. 2007;30(11):562–6. doi:10.1002/clc.20132.
18. Cai P, Peng Y, Chen Y, et al. Association of thyroid function with white coat hypertension and sustained hypertension. J Clin Hypertens (Greenwich). 2019;21(5):674–83. doi:10.1111/jch.13536.
19. Gutiérrez E, Flammer AJ, Lerman LO, Elízaga J, Lerman A, Fernández-Avilés F. Endothelial dysfunction over the course of coronary artery disease. Eur Heart J. 2013;34(41):3175–81. doi:10.1093/eurheartj/eht351.
20. Eid S, Sas KM, Abcouwer SF, et al. New insights into the mechanisms of diabetic complications: role of lipids and lipid metabolism. Diabetologia. 2019;62(9):1539–49. doi:10.1007/s00125-019-4959-1.
21. Engeli S, Stinkens R, Heise T, et al. Effect of Sacubitril/Valsartan on Exercise-Induced Lipid Metabolism in Patients With Obesity and Hypertension. Hypertension. 2018;71(1):70–7. doi:10.1161/HYPERTENSIONAHA.117.10224.
22. Prat H, Araos P, Michea L. La inflamación en la hipertensión arterial, mecanismos de producción e implicancias terapéuticas [Role of inflammation in hypertension]. Rev Med Chil. 2021;149(2):255–62. doi:10.4067/s0034-98872021000200255.
23. Carvalho DP, Dupuy C. Thyroid hormone biosynthesis and release. Mol Cell Endocrinol. 2017;458:6–15. doi:10.1016/j.mce.2017.01.038.
24. Fekete C, Lechan RM. Central regulation of hypothalamic-pituitary-thyroid axis under physiological and pathophysiological conditions. Endocr Rev. 2014;35(2):159–94. doi:10.1210/er.2013-1087.