2D SHEAR WAVE ELASTOGRAPHY OF NORMAL THYROID GLAND IN NEPALESE POPULATION

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ABSTRACT

Ultrasonography (USG) is modality of choice for normal, diffuse or nodular thyroid diseases. Two dimensional shear wave elastography (2D-SWE) is the latest innovation in USG techniques that allows real-time quantitative assessment of tissue stiffness using acoustic radiation force impulse (ARFI) induced by ultrafast focused US beam sequence (up to 20,000Hz) to record the propagation of the shear waves in real time and displays a map that represents the local elasticity values of tissues in real-time and in a quantitative manner without any compression of the organ. At times, there are difficulties in differentiating normal thyroid gland from diffuse thyroid disease based solely on gray scale USG for which 2D-SWE can be an adjunct. This study aims to establish 2D-SWE parameters for normal thyroid gland in Nepalese population. A cross sectional descriptive study was carried out with 2D SWE on all euthyroid patients with normal thyroid gland on B-mode USG at Department of Radiology, Nepal Medical College Teaching Hospital between December 2021 and November 2022. Tissue stiffness of normal thyroid gland was recorded and tabulated in terms of SMV units (m/s) according age and gender. Out of 100 subjects (52 females and 48 males) the youngest was 16 year female and oldest was 68 year female with mean age of 37.07 year (S.D = 11.58). Minimum mean velocity of 1.78 m/s was seen in 36 year old male and maximum of 3.40 m/s in 26 year old female. Mean of mean velocity was 2.36 m/s with (S.D= 0.34). Linear positive correlation was seen between shear wave velocities and age with no statistically significant difference between genders. This study had the most number of normal subjects (100) with almost equal gender distribution (52 females and 48 males) compared to previous studies in known literature. This study also analyzed correlation of shear wave velocity with age unlike other studies. Statistically significant correlation was seen between age and velocities in males only and also in mean velocities between age group 21-40 and 41-60 years (p-value= 0.037).

KEYWORDS

Thyroid gland, 2D shear wave elastography, shear wave velocity, strain modulus

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INTRODUCTION

Nepal lies in an area of endemic iodine deficiency and thyroid dysfunction, along with higher than average prevalence of goiter, is a major public health problem.[1] It has been estimated that 0.2% of the deaths in Nepal result from endocrine disorders, among which iodine deficiency is a major cause.[2] A hospital based study on thyroid dysfunction in Eastern Nepal in 2002 revealed that prevalence of hypothyroidism, hyperthyroidism and euthyroid was 17.19%, 13.68% and 69.11% respectively, with goiter with dysthyroidism being slightly more common among hill castes.[1] In a recent study in 2015 in Central Nepal, among 5,230 subjects, prevalence of thyroid dysfunction was 29.0% with subclinical hypothyroidism 17%, hypothyroidism 8%, hyperthyroidism 3%, subclinical hyperthyroidism 1% and euthyroidism 71%.[3] Another study in Western Nepal among 1504 subjects showed that the prevalence of thyroid dysfunction was 17.42%.[4] Females had more thyroid dysfunction than the males. Hypothyroidism (2.26%) and subclinical hypothyroidism (10.50%) had higher prevalence as compared to hyperthyroidism (1.59%) and subclinical hyperthyroidism (3.05%).

Ultrasonography (USG) is the most sensitive imaging modality available for diagnosing normal, diffuse or nodular thyroid diseases.[5] USG is non-invasive, widely available, less expensive, and does not use any ionizing radiation.[6] Two dimensional shear wave elastography (2D-SWE) is the latest innovation in USG techniques that allows real-time quantitative assessment of the medium stiffness.[7] It uses the acoustic radiation force impulse (ARFI) induced by a focused US beam to reach underlying tissues, and an ultrafast US sequence (up to 20,000Hz) to record the propagation of the shear waves in real time. It does not rely on external compression.[8] This ultrasound-based method can accurately evaluate the elasticity of superficial tissues such as the breast, prostate, scrotum, neck and thyroid.[9-11] In addition to visualization of elasticity on colour-coded elastographic images, the strain of tissues can be defined using numerical strain values and compared by cross- correlation of radiofrequency signals.[12] Shear wave elastography provides a great deal of precision and is perfectly suited to the study of this thyroid gland as it displays a map that represents the local elasticity values of tissues in real-time and in a quantitative manner without any compression of the organ.[13]

At times, there are difficulties in differentiating normal thyroid gland from diffuse thyroid disease based solely on grayscale USG. There have been many publications discussing the utility of 2D shear wave elastography in evaluation of thyroid nodules but only a few have discussed the appearance of normal thyroid tissue with this elastography technique. This study aims to study the role of 2D SW elastography in normal thyroid gland and establish parameters for the normal thyroid gland on 2D-SWE, record and tabulate tissue stiffness of normal thyroid gland in terms of SMV (m/s) units according age and gender, calculate and tabulate mean tissue stiffness of normal thyroid gland in each and both lobes of normal thyroid gland in Nepalese population.

MATERIALS AND METHODS

A descriptive cross sectional study was performed on 100 euthyroid patients of all age group and gender with normal thyroid gland on B- mode and Doppler USG underwent 2DSWE of the thyroid gland at Department of Radiology, Nepal Medical College Teaching Hospital, Attarkhel, Gokarneshwor-08, Kathmandu for a period of one year (December 2021 – November 2022). Patients with deranged thyroid function test , known thyroid diseases, history of thyroid surgeries and not giving consent were excluded from the study.

Approval from Nepal Medical College-Institutional Review committee (NMC-IRC) was taken before the conduction of the study. An informed consent of all the patients was taken, explaining the details of nature of the examination and the estimated duration of examination. Aplio™ 300 ultrasound machine (Toshiba Medical Systems Co. Ltd, Otawara, Japan) with linear 7.0 – 12.0 MHz transducer and elastography software was used. To avoid interobserver bias, the study was done by a single observer. Routine B-mode (dimensions and parenchymal echogenicity) ultrasound evaluation was performed prior to the ultrasound 2D SWE. Patients were asked to hold their breath for 5 seconds after normal inspiration for shear wave velocity (SWV) imaging. Transducer was placed gently over the skin without applying compression. Virtual touch tissue imaging Quantification (VTIQ) color maps were obtained in which the blue color shows soft and the red color shows hard tissue. On VTIQ maps, SWV (m/s) and its standard deviation (SD) were recorded from a normal thyroid parenchyma where the hardest and softest points are closest to each other at the same depth. Three separate VTIQ color maps was captured from each lobe (one each for upper, middle and lower poles), and the most appropriate one to perform

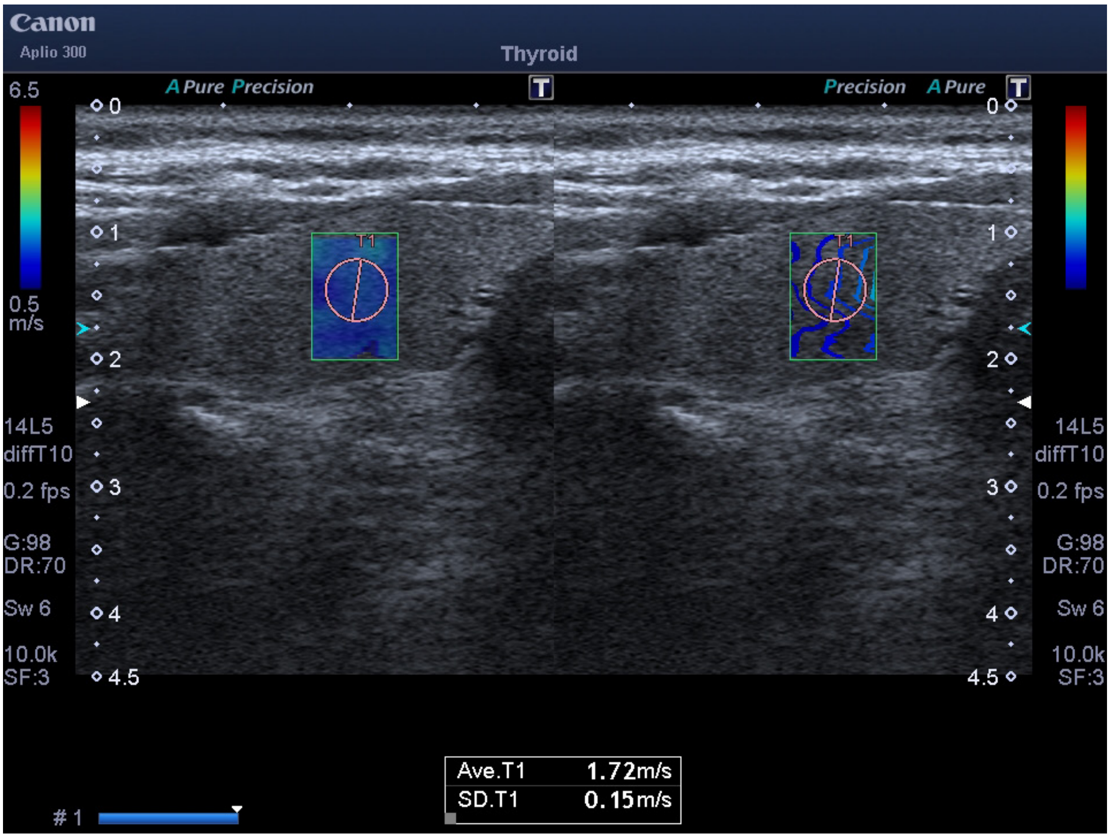

Fig. 1: 2D SWE VTIQ maps demonstrates shear wave velocity in normal thyroid gland. Note how the normal parenchyma is predominantly blue in color denoting softness.

SWV measurements was chosen (Fig.1). Care was taken not to include near field or bang artifacts. The maximum SWV value, measured from the hardest point, and minimum SWV value, measured from the softest point, and the difference between the minimum and maximum speed rate(Δv) and mean for each case was calculated. Six measurements from regions of interest , one each for upper, mid and lower pole from each lobe were taken. SWV (m/s) and strain modulus (k Pa) are interconvertible by the formula: Young's modulus (k Pa) = $3Cs^2$, where Cs is SWV.

The collected data was coded and entered in to Microsoft Excel. The Statistical Package for Social Sciences (SPSS)-16, software was used for the analysis of data. Categorical parameters was expressed as number and frequency. Quantitative parameters were expressed as mean ± standard deviation. Descriptive analysis was presented in numbers and percentages , analytical statistics was done using chi-square test.

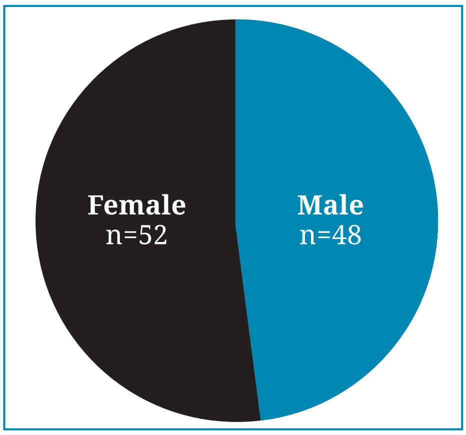

Fig. 2: Distribution according to gender.

RESULTS

Amongst total of 100 subjects , 52 were females and 48 were males (Fig.2). Youngest was 16 year old female and oldest was 68 year female. Mean age was 37.07 year (S.D = 11.58). Distribution of number of subjects according to age group was as follows; 0 to 20 year five , 21 to 40 year 56 , 41 to 60 year 37 and 61 to 80 two (Table 1). Table 2

Table 1: Frequency distribution based on different age groups.

Age Group (years)	(n)	%
0-20	5	5.0
21-40	56	56.0
41-60	37	37.0
61-80	2	2.0
Total	**100**	**100.0**

Table 2: Frequency distribution based on different age groups and gender.

Sex	Age range (years)				Total
	0-20	21-40	41-60	61-80	
Male	0	26	21	1	48
Female	5	30	16	1	52
Total	**5**	**56**	**37**	**2**	**100**

Table 3: Mean shear wave velocities in male and female subjects

	Sex	N	Mean (m/s)	Std. Deviation	Std. Error Mean
Mean velocity (m/s)	Male	48	2.40	0.34	0.049
	Female	52	2.33	0.35	0.048

Table 4: Distribution of mean shear wave velocities according to age group

Age range	Mean (m/s)	n	Std. deviation
0-20	2.4447	5	0.26128
21-40	2.2796	56	0.29650
41-60	2.4727	37	0.38722
61-80	2.7450	2	0.46905
Total	**2.3686**	**100**	**0.34646**

shows frequency distribution of subjects based on different age groups and gender.

Highest shear wave velocity of 3.90 m/s was obtained from right lower lobe in 26 year female and lowest velocity of 1.53 m/s in 36 year male. Minimum mean velocity of 1.78 m/s was seen in 36 year old male and maximum mean velocity of 3.40 m/s in 26 year old female. Mean of mean velocity was 2.36 m/s with standard deviation of 0.34. No statistically significant difference in mean velocity between male and female was noted (p=0.37) (Table 3).

In males, the range of velocities between the age of 21 to 40 years was 1.78 to 2.94 m/s, between 41 to 60 years was 1.92 to 3.18 m/s and between 61 to 80 years was 3.08cm/s which was single sample. Similarly in females, the range of velocities between the age of 0 to 20 years was 2.04-2.75 m/s, between 21 to 40 years was 1.78-3.40 m/s, between 41 to 60 years was 1.91-3.18 m/s and between 61 to 80 years was 2.41 m/s which was single sample.

Table 4 shows means shear velocities in different age groups. Statistically significant difference in mean shear wave velocities was seen between age group 21-40 and 41-60 (p=0.037), irrespective of gender, using one way ANOVA post hoc analysis test (Jenty). Significant positive correlation was also noted between age and velocities with Pearson's correlation coefficient of 0.24 (p=0.019). Significant correlation was seen between age and velocities in males only with Pearson's correlation coefficient of 0.34 (p=0.017). No significant correlation was seen between age and velocities in female with Pearson's correlation coefficient of 0.140 (p=0.55) but showed weak positive correlation.

DISCUSSION

Diffuse thyroid diseases like acute, subacute, chronic thyroiditis or goitre are more subtle on B mode USG than nodular thyroid disease. USG was recommended in the 2015 American Thyroid Association Management Guidelines for imaging thyroid nodules.[14] Ultrasound elastography is a sophisticated imaging technique that evaluates tissue stiffness.[15-17] 2DSWE imaging is an operator-independent, reproducible, and quantitative elastography technique.[18-20] Thyroid elastography makes it possible to improve the positive predictive value (PPV) and the negative predictive value (NPV) of malignancy obtained from conventional ultrasound studies.[21,22] Shear wave elastography makes it possible to objectively quantify tissue stiffness by providing a numerical value that varies between 1.82 and 3.65 m/s for healthy thyroid tissue. Several studies proposed this measurement for the characterization of non-nodular thyroid diseases.[23,24] Our study showed a range of 1.78-3.40 m/s, which is comparable to above studies.

A Romanian study by Sporea *et al*[25] on 136 subjects comprising of 44 normal, 48 Grave's disease (GD), 37 chronic autoimmune thyroiditis (CAT), four diffuse goiter and three amiodarone induced thyroid pathology patients, showed the normal values of thyroid gland tissue elastography to be about 2.01 ± 0.40 m/s but significantly increased stiffness in patients with GD (2.64 ± 0.52 m/s) and CAT (2.50 ± 0.56 m/s). Compared to above study, our mean shear wave velocity of 2.36 m/s is slightly higher , which could be due to lesser number of controls (44 subjects) , even though mean age in our study was younger (37.0 years) compared to theirs (45.8 years).

A study on 250 patients by Cepeha *et al*[26] using strain wave elastography, amongst which 70 were healthy subjects and 180 had CAT, concluded that the strain ratio (SR) (ratio of stiffness of thyroid parenchyma to adjacent sternocleidomastoid muscle) was significantly higher in (CAT) compared with the controls (2.81±2.11 vs 1.03±0.51; p <0.0001). This study evaluated 250 patients, 180 of them had CAT. The control group consisted of only 70 healthy subjects with lopsided female predominance (four males and 66 females). The mean of 40.8 years and mean velocity of 2.15 m/s was comparable to our study but the above study mainly focused on parenchyma/ sternocleidomastoid muscle strain ratios (SR) rather than absolute SMV values as in our study.

Sedlackova *et al*[27] compared the thyroid stiffness in 46 patients with diffuse thyroid pathology and 128 healthy patients. The range was 1.77 - 2.73 m/s with mean of 2.25 m/s which is lower but comparable to our study although the mean age of 50.8 years is much older than our study subjects.

Kara *et al*[28] also found significant differences between healthy and diffuse thyroid disease groups but, in addition, a positive correlation between SWE measurements and both anti-thyroid peroxidase (ATPO) and anti thyroglobulin (ATG) antibodies was noted as well as a significant negative association between SWE and echogenicity. Our study did not assess the echogenicity of the gland or correlate it with APTO and ATG.

Liu *et al*[29] studied thyroid stiffness in 30 normal subjects and 154 patients with diffuse thyroid disease (DTD) using SWE and found that stiffness was significantly greater in DTD compared with normal and concluded that SWE is superior to the fT3/fT4 ratio for distinguishing GD from SAT. However, SWE was unsuitable for differentiating CAT from GD.

Ruchala *et al*[30] have studied the role of sonoelastography in acute, subacute and chronic thyroiditis and concluded that thyroid tissue stiffness in subacute thyroiditis (SAT) gradually decreased over period time and with treatment. Baseline thyroid stiffness in SAT was higher than that found in CAT (3.47±2.49 m/s, P <0.0001) and control (2.32±1.34 m/s, P <0.0001). In the remission of SAT, thyroid stiffness was lower than that found in CAT (p =0.006), while it was higher than that in CS (p =0.0008). Patients with CAT presented higher thyroid stiffness than CS (p <0.0001), which was not influenced by L-thyroxine treatment. Thyroid stiffness in patients with acute thyroiditis (AT) was 8.49 and 8.97 m/s at baseline; after treatment, it decreased to 2.44 and 5.33 m/s respectively. This study used 36 women and only four men(total 40) aged 21–78 (median 47.5) years as control subjects. Shear velocity of normal thyroid gland in this study was similar to that of our study (2.32 vs 2.36 m/s), however our study did not evaluate diffuse thyroid disease or evaluate its response by elastography after treatment.

Our study demonstrated that there was linear positive correlation between age and SMV and it was statistically significant between age group 21-40 and 41-60 (p =0.037) particularly in males. This may be because a study has shown that with age the thyroid parenchyma becomes stiffer owing to fibrosis or fatty infiltration within the extracellular matrix.[31] Another study has shown that the basement membrane and the interstitial connective tissue significantly increased in correlation to age and interstitial fibrosis also increased with age due to age related increased content of collagen fibers.[32]

To our knowledge none of the previous studies have shown or analyzed correlation of age with SMV values of normal thyroid parenchyma. Our study have not only shown positive correlation of SMV with age but also inference could be made that thyroid parenchyma becomes significantly stiffer after age of 40 years based solely on 2DSWE values, especially in males. However no statistically significant difference in mean velocity between male and female was noted (p =0.37) in our study.

In conclusion, compared to all the previous studies mentioned above our study had the most number of normal subjects (100) with almost equal gender distribution (52 females and 48 males). Hence, we can assume that our study is more representative of normal thyroid elastography in general population. Although much larger population cross section is necessary to more accurately establish representative SMV values for normal thyroid gland.

Conflict of interest: none

Source of research fund: none

REFERENCES

1. Baral N, Lamsal M, Koner BC, Koirala S. Thyroid dysfunction in Eastern Nepal. *Southeast Asian J Trop Med Public Health* 2002; 33: 638-41.
2. Ganie MA, Zargar AH. Scenario of endocrinology in South Asia. *Indian J Endocrinol Metabol* 2007; 11: 1-2.
3. Mahato RV, Jha B, Singh KP, Yadav BK, Shah SK, Lamsal M. Status of thyroid disorders in central Nepal: a tertiary care hospital based study. *Int J Appl Sci Biotechnol* 2015; 3: 119-22.
4. Yadav RK, Magar NT, Poudel B, Yadav NK ,Yadav B. A prevalence of thyroid disorder in western part of Nepal. *J Clin Diagn Res* 2013; 7: 193-6.
5. Chaudhary V, Bano S. Imaging of the thyroid: Recent advances. *Indian J Endocrinol Metab* 2012; 16: 371-6.
6. Friedman AC. Book Review Diagnostic Ultrasound. Second Edition. *N Engl J Med* 1998; 338: 1080-1.
7. Bouchet P, Gennisson JL, Podda A, Alilet M, Carrié M, Aubry S. Artifacts and technical restrictions in 2D shear wave elastography. *Ultraschall Med* 2020; 41: 267-77.
8. Chang JM, MoonWK, Cho N *et al*. Clinical application of shear wave elastography (SWE) in the diagnosis of benign and malignant breast diseases. *Breast Cancer Res Treat* 2011; 129: 89-97.
9. Koizumi Y, Hirooka M, Kisaka Y *et al*. Liver fibrosis in patients with chronic hepatitis C: noninvasive diagnosis by means of real-time tissue elastography-establishment of the method for measurement. *Radiol* 2011; 258: 610-7.
10. Fleury E, Fleury, J, Piato CV, Roveda D Jr. New elastographic classification of breast lesions during and after compression. *Diagn Interv Radiol* 2009; 15: 96-103.
11. Wojcinski S, Cassel M, Farrokh A *et al*. Variations in the elasticity of breast tissue during the menstrual cycle determined by real-time sonoelastography. *J Med Ultrasound* 2012; 31: 63-72.
12. Onur MR, Poyraz AK, Ucak EE, Bozgeyik Z, Özercan IH, Ogur E. Semiquantitative strain elastography of liver masses. *J Ultrasound Med* 2012; 31: 1061-7.
13. Bhatia KSS, Cho CCM, Tong CSL, Yuen HK. Shear wave elasticity imaging of cervical lymph nodes. *Ultrasound Med Biol* 2012; 38: 195-201.
14. Haugen BR, Alexander EK, Bible KC *et al*. 2015 American thyroid association management guidelines for adult patients with thyroid nodules and differentiated thyroid cancer: the American Thyroid Association Guidelines Task Force on Thyroid Nodules and Differentiated Thyroid Cancer. *Thyroid* 2016; 26: 1-133.
15. Shao J, ShenY, Lü J, Wang J. Ultrasound scoring in combination with ultrasound elastography for differentiating benign and malignant thyroid nodules. *Clin Endocrinol (Oxf)* 2015; 83: 254-60.
16. Chen L, ZhangJ, Meng L, Lai, Y, Huang, W. A new ultrasound nomogram for differentiating benign and malignant thyroid nodules. *Clin Endocrinol* (Oxf) 2019; 90: 351-9.
17. Sun J, Cai J, Wang X. Real-time ultrasound elastography for differentiation of benign and malignant thyroid nodules. *J Ultrasound Med* 2014; 33: 495-502.
18. Zhao CK, Chen SG, Alizad A *et al*. Three-dimensional shear wave elastography for differentiating benign from malignant thyroid nodules. *J Ultrasound Med* 2018; 37: 1777-88.
19. Hegedüs L. Can elastography stretch our understanding of thyroid histomorphology? *J Clin Endocrinol Metab* 2010; 95: 5213–5.
20. Grant, EG, Tessler FN, Hoang JK *et al*. Thyroid Ultrasound Reporting Lexicon: White Paper of the ACR Thyroid Imaging, Reporting and Data System (TIRADS) Committee. *J Am Coll Radiol* 2015; 12: 1272-9.
21. Asteria C, Giovanardi A, Pizzocaro A *et al*. US-Elastography in the Differential Diagnosis of Benign and Malignant Thyroid Nodules. *Thyroid* 2008; 18: 523-31.
22. Schott M. US-elastography in the differential diagnosis of benign and malignant thyroid nodules. *Yearbook Endocrinol* 2009; 157-8.
23. Magri F, Chytiris S, Capelli V *et al*. Shear wave elastography in the diagnosis of thyroid nodules: feasibility inthe case of coexistent chronic autoimmune Hashimoto's thyroiditis. *Clin Endocrinol (Oxf)* 2012; 76: 137-41.
24. Liu B, Liang j, Zhou L *et al*. Shear wave elastography in the diagnosis of thyroid nodules with coexistent chronic autoimmune Hashimoto's thyroiditis. *Otolaryngol Head Neck Surg* 2015; 153: 779-85.
25. Sporea I, Sirli R, Bota S *et al*. ARFI elastography for the evaluation of diffuse thyroid gland pathology: Preliminary results. *World J Radiol* 2012; 4: 174-8.
26. Cepeha CM, Paul C, Borlea A *et al*. The value of strain elastography in predicting autoimmune thyroiditis. *Diagnostics (Basel)* 2020; 10: 874.
27. Sedlackova Z, Herman J, Furst T *et al*. Shear wave elastography in diffuse thyroid disease. *Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub* 2021; 165: 152-6.
28. Kara T, Ateş F, Durmaz MS *et al*. Assessment of thyroid gland elasticity with shear-wave elastography in Hashimoto's thyroiditis patients. *J Ultrasound* 2020; 23: 543–51.
29. Liu J, Zhang Y, Ji Y, Wan Q, Dun G . The value of shear wave elastography in diffuse thyroid disease. *Clin Imaging* 2018; 49: 187-92.
30. Ruchala M, Parulska ES, Zybek A *et al*. The role of sonoelastography in acute, subacute and chronic thyroiditis: a novel application of the method. *Eur J Endocrinol* 2012; 166: 425-32.
31. Lee J, Yi S, Kang YE *et al*. Morphological and functional changes in the thyroid follicles of the aged murine and humans. *J Pathol Transl Med* 2016; 50: 426-35.
32. Abdullah SI, Abdul-Jabbar J, Samarrae Al *et al*. The effect of aging on human thyroid gland: anatomical and histological study. *Iraqi J Comm Med* 2010; 23: 158-64.