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## Study of technetium pertechnetate(<sup>99m</sup>TcO<sub>4</sub>) thyroid scintigraphy imaging among patients presenting with thyrotoxicosis at a tertiary care hospital in Kathmandu, Nepal

<sup>1</sup>Mall D, <sup>1</sup>Maharjan S, Rajouriya AD, Karki BB, Shrestha PS, Shrestha C, <sup>2</sup>Shrestha D, Bajracharya MR  
<sup>1</sup>National Academy of Health Sciences, Kathmandu, Nepal, Bir Hospital, <sup>2</sup>Norvic International Hospital

**Background:** Thyroid disorders represent an important public health problem worldwide. Excess thyroid hormone in the circulation due to any cause is termed as thyrotoxicosis. There are many causes of thyrotoxicosis, and it is important to find the cause as this will determine the management of the condition. <sup>99m</sup>TcO<sub>4</sub> scintigraphy is a diagnostic tool to differentiate various causes of thyrotoxicosis. This study aims to study the age and gender distribution of different causes of thyrotoxicosis. **Methods:** This is a retrospective analysis of technetium pertechnetate(<sup>99m</sup>TcO<sub>4</sub>) thyroid scintigraphy reports done of patients having thyrotoxicosis from the period of January 01, 2016, to December 31, 2016, at the Nuclear Medicine unit of National Academy of Medical Sciences, Bir Hospital, Kathmandu. Gender and age group analysis of the data was done using SPSS program. **Results:** A total of 211 reports of <sup>99m</sup>TcO<sub>4</sub> thyroid scintigraphy were included in the study. There were 61 male patients and 150 female patients. Various causes of thyrotoxicosis like thyroiditis, Graves' disease, autonomous functioning thyroid nodule, toxic multinodular goiter was detected. Apart from toxic multinodular goiter, these disorders were more common in the age group 18-50 years and females. **Conclusion:** <sup>99m</sup>TcO<sub>4</sub> thyroid scintigraphy is one of the easy and highly effective tools for the differential diagnosis of thyrotoxicosis. Both thyroiditis and Graves' disease are more predominant in the age group 18-50 years and in females. Further large community-based studies will be required for exact prevalence of the diseases in the population.

Key Words: hyperthyroidism, Graves' disease, thyroiditis, thyrotoxicosis, <sup>99m</sup>TcO<sub>4</sub> Scan

### Introduction

Thyroid disorders represent an important public health problem worldwide. Thyrotoxicosis is the term applied to a health condition when there is excess thyroid hormone in the circulation due to any cause. Thyrotoxicosis can be easily diagnosed by a high serum level of thyroxine (T<sub>4</sub>) and triiodothyronine (T<sub>3</sub>) and a low serum level of TSH.<sup>1</sup> Subclinical thyrotoxicosis is a condition when serum T<sub>3</sub> and T<sub>4</sub> are within normal range and TSH is undetectable.<sup>2</sup> Thyrotoxicosis is not synonymous with hyperthyroidism which is a

result of excessive thyroid function. However, the major causes of thyrotoxicosis are hyperthyroidism caused by Graves' disease, toxic multinodular goiter (TMNG) and Autonomous Functioning Thyroid Nodules (AFTN) or toxic adenomas.<sup>1</sup>

According to a meta-analysis done in Europe, prevalence of hyperthyroidism was found to be 0.8%.<sup>3</sup> Thyrotoxicosis is also common in the Australian community.<sup>4</sup> A study from eastern Nepal showed that out of a total of 599 patients, 13.68% were affected by hyperthyroidism whereas another cross sectional study done in a district hospital in Bayalpatha, Nepal showed thyroid disorders to be present in 17% of the study population with approximately one fourth having hyperthyroidism.<sup>5,6</sup> In a population survey done by Carlos et al. involving almost 5000 non pregnant adults it was seen that subclinical

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### Correspondence Author

Dr. Dipak Malla  
National Academy of Health Sciences, Kathmandu, Nepal  
email: drdmalla@hotmail.com

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hyperthyroidism was present in 5.33% where as true hyperthyroidism was seen in only 0.61%.<sup>7</sup>A population study in the US showed hyperthyroidism to be present in 1.3% (0.5% clinical and 0.7% subclinical).<sup>8</sup> Various other studies done in different parts of Nepal has shown that the prevalence of overt hyperthyroidism ranged from more than 2% to 14.9% and subclinical hyperthyroidism from 1% to almost 10%.<sup>9-12</sup>

To treat thyrotoxicosis appropriately, determining the cause is essential as the selection of treatment differs according to the cause of thyrotoxicosis and the wishes of the individual patient.<sup>1,4</sup> Antithyroid drugs, radioactive iodine, and surgery are the three treatment options for the 3 common forms of hyperthyroidism.<sup>1</sup> Radionuclide imaging has been an important part of the thyroid evaluation for many years and following biochemical confirmation of thyrotoxicosis, a radionuclide thyroid scan is the most useful investigation in diagnosing the underlying cause.<sup>4, 13,14</sup> Radionuclide scans can provide information about the size, shape of the thyroid gland and it can also be helpful to detect retrosternal goiter and ectopic thyroid tissue.<sup>14-16</sup> It helps to diagnose thyroid diseases on the basis of level of radiotracer uptake in thyroid gland.<sup>16</sup>

Graves' disease, TMNG, AFTN are causes of hyperthyroidism. The radionuclide uptake scan can easily differentiate the high uptake of hyperthyroidism from the low uptake of thyroiditis in cases of thyrotoxicosis. In thyroiditis, there is destruction of thyroid follicles with the release of preformed thyroid hormones.<sup>1,17,18</sup> From a molecular point of view, the uptake of radioiodine and pertechnetate is proportional to the expression of the thyroidal sodium/iodine symporter.<sup>19</sup> For scanning purposes,  $^{99m}\text{TcO}_4$  scans have become more popular because sufficiently mimics the behavior of iodine.<sup>20</sup> The assessment of thyroid structure, location and function using  $^{99m}\text{TcO}_4$  is simple, readily available, uses lower radiation doses, fast and cost efficient method, which could easily become a part of the routine studies in nuclear medicine laboratories.<sup>13,16,20,21</sup> Nuclear scanning with  $^{99m}\text{TcO}_4$  as the main diagnostic radionuclide

is also used for thyroid scans in Australia.<sup>4</sup>

The number of patients with thyroid disorders is increasing every day. As biochemical testing for thyroid disorder became easier more and more patients are being found to have thyroid dysfunction. There are hardly any studies in our country regarding the etiology of various causes of thyrotoxicosis hence this study was carried out.

### Methods

This was a retrospective analysis of  $^{99m}\text{TcO}_4$  thyroid scintigraphy reports done for thyrotoxicosis from the January 1st 2016 to December 31st 2016 at the Nuclear Medicine Unit of National Academy of Medical Sciences, Bir Hospital. Ethical approval for the study was approved by the Institutional Review Board.

Vast majority of patients in the study were referred from the Diabetes and Endocrine Unit of Bir Hospital for evaluation of overt or subclinical thyrotoxicosis. The medical equipment used for the nuclear scan was Nucline<sup>TM</sup> SPIRIT DH-V Dual Head SPECT gamma camera from Mediso Medical Imaging Systems, Hungary. Radiopharmaceutical used for the study was  $^{99m}\text{TcO}_4$  and a dose of 3-5 mCi was given intravenously followed by imaging with the gamma camera after 20 minutes of the administration of the radiopharmaceutical. The system was fitted to a computer system which enabled to determine of uptake of the  $^{99m}\text{TcO}_4$  as an iodine clearance equivalent.<sup>19</sup> Percentage uptake of tracer in thyroid was measured. If patients were taking anti-thyroid drug, the same was stopped for at least 3 days prior to scan.

Regarding interpretation of scans, in Graves' disease there is diffuse increased uptake (diffused toxic goiter, DTG).<sup>16,22,23</sup> Depending upon clinical scenario and hormonal profile, a diffuse uptake in normal range was also considered as consistent with diffuse toxic goiter. The uptake would be normal or high with an asymmetrical and irregular nodular pattern in TMNG. AFTN is independent of TSH control and the image will shows focal increased

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tracer uptake confined to a nodule that occupies most or all of the thyroid lobe and the remaining gland will be non-visualized due to total suppression of TSH stimulation.<sup>16,22</sup> The radionuclide uptake will be low in cases of thyroiditis.<sup>1, 17</sup>

Inconclusive reports were not included in the study. Drug induced thyrotoxicosis were also excluded from the study. Analysis was done for gender and age distribution for thyroid disorders like Graves' disease, thyroiditis, TMNG, AFTN among thyrotoxicosis patients. SPSS 20.0 tools were used for data analysis.

**Results**

According to the inclusion criteria, they were a total 211 patients who had undergone <sup>99m</sup>TcO<sub>4</sub> thyroid scintigraphy for thyrotoxicosis. The mean age of the patients were 38.50 years in general. The study had 150 females, 61 male patients and the mean age of male and female patients were also similar, 38.36 years and 38.56 years respectively. There were 113 patients with thyroiditis, 87 patients with Graves' disease or DTG, 9 patients with AFTN and 2 patients with TMNG. So, thyrotoxicosis due to hyperthyroidism (Graves' disease, AFTN, TMNG) were a total of 98 cases of which females were 68 and males were 30 making a female male ratio of 2.2 :1.

**Table 1. Age and gender distribution of patients with diffuse toxic goiter**

Age in years	Number of patients	Male	Female
18-29	27	10	17
30-39	20	5	15
40-49	21	5	16
50-59	9	4	5
60-69	7	0	7
70-79	1	1	0
More than 80	2	0	2
Total	87	25	62
<b>Mean age</b>	<b>39.33</b>	<b>36.04</b>	<b>40.66</b>

Most of the diffuse toxic goiter or Graves' Disease patients were in the age group 18-50 years making 68 (78%). It is seen that most of the patients 20 (80%) of the male and 48 (77%) of the female patients with diffused toxic goiter were also below the age of 50 years. The female to male ratio was almost 2.5 times for Graves' disease.

**Table 2. Age and gender distribution of patients with thyroiditis**

Age years	Number of patients	Male	Female
18-29	32	6	26
30-39	33	10	23
40-49	25	7	18
50-59	16	6	10
60-69	4	1	3
70-79	3	1	2
Total	113	31	82
<b>Mean age</b>	<b>37.97</b>	<b>40.03</b>	<b>37.20</b>

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From Table 2 it is seen that the female to male ratio with those having thyroiditis were 2.6 :1. It is seen that many of the patients with thyroiditis were also in the age group 18-50 years comprising almost 67 ( 81.7 % ) of the female and 23 ( 74.1%) of the male patients .

**Table 3 . Age and gender distribution of patients with Autonomous functioning thyroid nodule**

Age years	Number of patients	Male	Female
18-29	3	1	2
30-39	2	2	0
40-49	4	1	3
Total	9	4	5
<b>Mean age</b>	<b>34.89</b>	<b>33.25</b>	<b>36.20</b>

From Table 3 in the AFTN group also females were slightly more than the males ( 5 vs 4 ) .The mean age from all the three disorders Graves’ disease , thyroiditis and AFTN were also similar being approximately in the range of 30-40 years. They were 2 patients with toxic multinodular goiter , one 32-year-old female and the other male patient age 65 years.

**Discussion:**

Thyroid function disorders are one of the most common endocrine disorders worldwide. In iodine-replete communities, the prevalence of hyperthyroidism in women is between 0.5 and 2%, and is 10 times more common in women than in men.<sup>24, 25</sup> According to Cooper DS, Graves’ disease is the commonest cause of hyperthyroidism followed by toxic nodular goiter.<sup>26</sup>

Graves’ disease, TMNG, AFTN and thyroiditis account for most presentations of thyrotoxicosis in Australia which is similar to our study although the number of cases of AFTN and TMNG are not very high.<sup>4</sup>

In our study also, thyrotoxicosis was mostly found among females. Similar results of more females being affected with hyperthyroidism was also seen in a study done by Taher MB et al in 2014 at the University of Maidu Guri Teaching Hospital, Nigeria.<sup>27</sup> In a research done in eastern Nepal , 69 females and 13 males were found to have hyperthyroidism. The vast majority of the patients were in the age group less than 50 years.<sup>5</sup> In our study the age group most affected was 18-50 years with a decline in prevalence with increasing age.

Thyroiditis most commonly affects women of 20-40 years.<sup>2,28</sup> Thyroiditis associated with viral

infections is also commonly seen in North America .<sup>2</sup> In our study also the mean age group of those with thyroiditis was 38 years with female to male ratio of 2.6 :1 . The female to male ratio for unspecified thyroiditis was 2.4:1 in the study done by Kantanka et al but in that study the mean age was on the higher side with 56 years.<sup>29</sup> Specific therapy is usually not warranted in cases of thyroiditis, however, treatment directed at symptoms may be required such as beta-adrenergic blocking agents are used in most patients for symptomatic relief and might be the only treatment needed for thyroiditis, which is transient.<sup>4, 26</sup> However pain associated with subacute thyroiditis may be relieved with the use of a nonsteroidal anti-inflammatory drug and in severe pain ,steroids may be used.<sup>18</sup>

Graves’ disease is commonest form of hyperthyroidism usually found in the age group 20 to 50 years with female patients being involved 5-10 times more than male patients.<sup>2,14,30,31</sup> In the study by Kantanka et al , diffuse toxic goiter accounted for only 12.1% of the admission for thyroid disorders with mean age of 37 years and female to male ratio of almost 5 times.<sup>29</sup> The mean age and predominance of Graves’ disease in females are similar to that of our study although the female to male ratio is 2.5 times in our study.

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iodine deficiency and iodine excess can result in an increased prevalence of thyroid disorders.<sup>33</sup> An epidemiological study done in a dietary iodine sufficient population in Scotland revealed that hyperthyroidism was five times more common in females as compared to males.<sup>34</sup> In a prospective study done in Denmark, it was observed that the incidence of mild hyperthyroidism is also reported to be higher in iodine-deficient areas than in iodine-sufficient areas and to decrease after introduction of universal salt iodization programmes.<sup>35</sup> A long study from Ghana however confirmed that iodine supplementation especially in regions of moderate-severe iodine deficiency increased the incidence of overt hyperthyroidism from toxic adenoma, toxic multinodular goiter and Graves' disease.<sup>29</sup> From a study by Laurberg et al it was seen that although in iodine-sufficient areas about 80% of patients with hyperthyroidism had Graves' disease, toxic multinodular goitre and toxic adenoma accounted for 50% of all cases of hyperthyroidism in iodine-deficient areas.<sup>36</sup>

According to the 2016 Nepal Demographic and Health Survey, after the initiation of iodized salt program, 96.9 percent of the urban household used iodized salt whereas in the rural area household it was 91.8 percent.<sup>37</sup> Studies done in school children in Nepal have revealed that approximately one third of the school children had excess urinary iodine concentration.<sup>38,39</sup>

This is quite alarming as even minor differences in iodine intake between populations are associated with differences in the occurrence of thyroid disorders. Therefore regular monitoring, assessment and adjusting of iodine intake in a population is an important part of preventive medicine.<sup>36,38,39</sup>

### Limitations of study

The study did not involve all the patients with thyrotoxicosis coming to the Diabetes and Endocrine Unit for treatment and only included cases that had undergone <sup>99m</sup>TcO<sub>4</sub> scan. Graves' disease or thyroiditis that were clinically apparent did not require to undergo a radionuclide scan and thus were not included in the study. The study also did not include patients who might have required

<sup>99m</sup>TcO<sub>4</sub> scintigraphy imaging for diagnosing the cause of thyrotoxicosis but was not done due to various reasons such as costs, pregnancy etc. The findings of this study only reflects that of those seeking treatment at a tertiary care hospital and thus cannot reflect the disease scenario in the community. Although the prevalence of the various causes of thyrotoxicosis cannot be estimated from this study however the study does give some information regarding high incidence of thyroiditis and the gender and age group predominance within various causes of thyrotoxicosis. This study can thus provide important data for further research.

### Conclusion:

<sup>99m</sup>TcO<sub>4</sub> thyroid scintigraphy is one of the easy and highly effective tools for the differential diagnosis of thyrotoxicosis. Both thyroiditis and Graves' disease are more predominant in the age group 18-50 years and in females. Further large community-based studies will be required for exact prevalence of the disease in the population.



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### Declarations

#### List of abbreviations

TCO-Techneium pertechnetate  
TMNG- Toxic multinodular goiter  
AFTN- Autonomous Functioning Thyroid Nodules  
T3-Triiodothyronine  
T4-Thyroxine  
TSH-Thyroid stimulating Hormone

#### Ethics approval and consent to participate

The study was conducted after the ethical approval from Institutional Review Committee, National Academy of Medical sciences, Bir Hospital, Nepal. Participants were explained about the research detail, its significance, the benefit and harm in Nepali language before obtaining the consent, their queries were answered. A statement indicating that the participants has understood all the information in the consent form and is willing to participate voluntarily was obtained. Participants were able to withdraw from the study at any time without giving any reason during the study period. The confidentiality of participants was assured and code number was used in each interview schedule and name of the participants was not mentioned anywhere.

#### Consent for publication

Not applicable

#### Competing interests

The authors declare that they have no competing interests.

#### Funding

Not applicable

#### Authors' contributions

ND conceptualized, collected data, analyzed and wrote the manuscript. BP supervised and guided throughout the study from the beginning of the study and critically reviewed the manuscript. All authors read and approved the final manuscript.

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