



## A Thyroid Carcinoma Induced by COVID-19 and its Effect on The Variation of Thyroglobulin Level as a Marker for Diagnosis and Assessment Strategy

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### ABSTRACT

**Background:** the thyroid carcinoma is one of the most cases seen of the thyroid un expected disease. Due to its increase in the no of cases reported there is un urgent interest of the prognostic risk expectations and the out come of the treatment. there will be an increment of the cases and an interesting in prohibit its complications by follow-up this disease. Aim: is to predict the effect of the thymoglobulin test in facilitating its diagnosis in consideration with selectivity and the specify. Results: data indicated that although this test is helpful in the diagnosis but still it is not only deoendable test used due to lack of complete accuracy in different cases of the thyroid disease. one of the main reasons for the thyroid carcinoma is viral infection, particularly COVID due its effect on the endocrine function of the human body especially thyroid gland and its abnormally proliferation and behavior that could be ends with tumors even if this tumor is multifactorial but there is and evedance that it caused by viral infection

**Keywords:** Thyroglobulin, Thyrotropin, Papillary thyroid carcinoma, Follicular carcinoma, Thyroidectomy, Radioactive iodine, Radioimmunoassay.

### Article Information

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## INTRODUCTION

Papillary thyroid tumor: a tumor that occurred in the thyroid gland in more than seventy percent of the total thyroid case that had been reported. It tends to occur more in females than males, the explanations are controversial but still more occurred in females than in males and more in coupled that how lived in one places especially in the modern arias than in rural one. The hormonal changes with the age is one of the explanations that it more attack in those between twenty-two to the post-menopausal ages. Many reasine that could be ends with thyroid tumore especially the viral infection and it could be One of the most common cases is the exposure of the neck or head to radiation and many cases had been recorded in females that how to undergo US examination. Ironically, Some of the doctors called this tumor is the flu of the tumor (1,2)

### Diagnosis:

It is recommended to perform a routine check-up at the ages of 25-60 years, weather to access the occurrence of sold or soft mass, pain, enlargement of the neckor even biochemical

markers. It could be proved in biopsy for the spiration of the sample especially if there is a sudden enlargement in size that is seen in the neck or diagnosed in the ultrasound. The last one

is used initially used to see whether the tissue is solid or soft (cyst) and to determine the size which could reach to less than one centimeter or 1.5 centimeter in length or enlargement of the lymph node in the cervix and assessment of the trachea (3) some of these cases could be solved by surgery and they may or may not require the surgery which includes total or partial removal of the gland (thyroidectomy), some of them end with radiotherapy (radioactive iodine therapy) and some of them not (4).

One of the other markers that may be used is thyroglobulin (it is a protein that is excreted from follicular cells and its increment may indicate the occurrence of the thyroid carcinoma whether it is due to papillary or follicular while the low concentration in the blood may indicate the presence of the antibodies of thyroglobulin) which may be regarded as a tumor marker. The staining of the human bone marrow endothelium marker which is used to distinguish between the carcinoma of the follicular and papillary cells and there are many other markers that may be used as an early diagnostic marker particularly the ATP5E (5).

Gene analysis (example microRNA) may be regarded as diagnostic between the carcinoma of the papillary glands and the benign nodules (6). This tumor also called lateral aberrant thyroid which means an invasion of the thyroid tumor to the lymph nodes and rarely invading the blood streams. This tends to be either encapsulated which tends to be benign or non-encapsulated and the follicular thyroid carcinoma is mostly the invasive type that may metastasize to the blood, lung, bones or even reach the head that it may need an urgent action (7).

### **The incidence of the mutation:**

This carcinoma tends to be either translocation or could be chromosomal and may be even the point mutation. The second one chromosomal mutation may be due to mutation at the chromosome number ten at the long arm telomere (q) at the position eleven. And it represents about twenty percent of the total types of carcinoma (8).

### **Treatment:**

As mentioned previously, the surgery (whether partial or even total removal of the thyroid gland) is regarded as the first-line strategy according to the guideline of the American Association 2009. Sometimes the surgery may be sufficient and not followed by the radiation (especially if there is no node or neck due to the small diameter of the tissue) and sometimes it may require the intake of radioactive iodine therapy whether it is ten or twenty or even more millicurie and this depends on one the report of the laboratory biopsy. If the diameter is more than one centimeter it is better to induce total removal of the thyroid gland with removal of the lymph nodes surrounding the tissue followed by radiation therapy is the better choice (9).

The follow-up of the occurrence of the cancer is more easily to be performed especially if the tumor size does not exceed four centimeters with no invasion or metastasis and the sensitivity and even the specificity of the test is increased after the total thyroidectomy particularly using the radioactive iodine 131. This total thyroidectomy makes it more easy to get a full decision after the US detects the metastasis and also less post-surgery complication and long-term consequences after the total thyroidectomy than the partial one (9) most patients with papillary carcinoma seem more aggressive with age and may reach to a level of very severe risk at age of more than forty five and not only require the removal of the thyroid but also removal of the all the surrounding of the lymph nodes and may even progress in to removal part of the trachea. While those with low risk cancer seem to respond very well to the treatment after thyroidectomy (10).

It may require a radiation therapy after four to six weeks after about one to months and after proven the removal of all of the thyroid tissue and the tumor cell that had been proved by total iodine scan finally a hormone replacement treatment is started for life using the levothyroxine to replace the daily requirement of the thyroxine and in order to avoid the cases of hypothyroidism. Routine check up of the thyroid tissue that it may remain is occurred

using different analysis, including the anti-thymoglobulin Abs and the thymoglobulin (11).

Nowadays the chemotherapy is low used in this kind of tumor particularly if there is metastasis to the bone and in this cases the treatment may be needed to facilitate the life quality. This chemotherapy may be required to inhibit the further cell growth and metabolic pathways in the normal tissue (12).

**Thymoglobulin:** it is a protein with molecular weight about six hundred and sixty kilodalton produced primarily by follicular cells of a gland, its level increases in carcinoma of the thyroid gland follicular and papillary (13). Thymoglobulin test is nowadays widely and simply used for tumor to follow the thyroid tumor because it is usually regarded as a marker of the cancer due to it is secreted by the tumor tissue or normal one. If the course of the treatment is correct, and the level of the thymoglobulin is not reduced to undetectable level or remain normal or even increase it means that it is still secreted by the tissue which could mean it is secreted by thyroid tumor cells. Normally it should be reduced to undetectable level since it is supposed that there is no normal tissue that secretes the thymoglobulin nor a tumor tissue that secretes it (14).

The normal value varies between male and female, in male it varies between 1.45 and more than 29.2 nano-gram per milliliter while in female it varies between 1.5 to more than 38.5 nano-gram per milliliter. The variation in result could be explained as the following (15):

**First:** if the level is high it could mean that there is a tissue (normal) that is not successfully removed by the surgery or there is a tumor cell that secretes this tumor marker.

**Second:** no level of undetectable or even very low: it means that there is no thyroid tissue in the body and all the tissue whether tumor or normal one is removed.

**Third:** if it decreases then started to increase: it may mean that the tumor is restarted to growing again and may need the medical care.

### Measurement of thymoglobulin:

It could be assessed by immunoassay, radioimmunoassay, chromatography spectrometric method. The second one is the most commonly used due to that it is more sensitive, shorter time required for incubation, the reagents are more stable, and the percent of error is very rare and finally the range of accuracy is wide.

### The aim of the study:

This review study aimed the evaluation of thymoglobulin as a marker to evaluate the degree of progress of the response after thyroidectomy.

### RESULTS AND DISCUSSION

This review article was conducted using some of the studies of the degree of the follow up of the thyroid carcinoma cases. Although the dependence on its level is not crucial for diagnosis of the tumor, but still it could be a good indicator for high activity of the tissue that secretes this protein. Its level is high for after operation and subsided down to an undetectable level after a month, but it takes many months to be completely undetectable. This hormone assessment may be useful during the intake of thyroid therapy after surgery, any test of stimulation of the thyroid stimulating hormone. Its level is an important alerting agent for as a guideline for observational studies and making a decision about the next step in the treatment, particularly after the operation and radioactive iodine treatment and even after a radioactive iodine test management. Not only that but also it is used during the treatment especially if its level exceeds the ten nanogram per milliliter which increases the probability of recurrence of the tumor (17).

The presence of the remnant tissue of tumor or normal thyroid cells may give an alert of another US assessment or another testing of tumor cells by total radioactive iodine test. It should be kept in mind that the measurement of the level of Tg is not only a (bad messenger) of a badly metastasized tumor, but it is also regarded as a good carrying news marker due to that its low level indicates the good prognosis of the cancer as it may be reduced to less than one nanogram per

milliliter. In general and to be fair we should not consider the Tg assay is a interesting factor of the evaluation and follow of the tumor cells science there are multi-factorial aspects that may vitiate its level (18).

Still, some studies prefer to ignore the dependence on the level of radio iodine assay in patient that showed a level less than 1 nanogram per mil level (19). Another studies suggest that low level with no enlargement of the nodules not required that radiation treatment. On the other hand, it used for those of low to high risk and give high level of readings and its correlation with the successful of the operation as a degree of operational failure is increase with level of Tg more than six nanogram per milliliter (20,21), Another aspect is the measurement the ratio of the thyroglobulin to the thyrotropin radio (Tg/Tr) with the result of the surgical operation. Some of the studies indicate the effective assessment of this results to the relation of the surgery in relation of the prognosis of the tumor and we can say that this ratio gives a useful dussion about what is best for the patient (22).

Another study suggested that Tg and the Tg/Tr ratio is unrelated to the outcome of the surgery while there is controversy of the results may be seen due to that in one had it suggest there might be a useful prediction of this ratio or at least the Tg value to the follow-up of the successful of the surgery while on the other hand there is some pitfall in the prediction of non usefulness of this to markers and eve it suggest to re-operation to confirm the disappearance of the tumor or even remnant tissue depending of previously discussed researches (23).

According to one of the studies, more that seven hundred patient had been included and the results was the pendance on the ratio of Tg to the TSH as a useful marker for the tumor assessment, and it is more dependant that evaluation of the Tg value alone, and the last ratio was used as more indicative of the failure and success of the operation. According to that results, the high level of the ratio, the more failure of the post operation of the radiation therapy. While when there is decrement of the Tgvalue may not indicate this failure (24,25). Another study suggested that this ratio is more accurate in diagnosis of the failure of the

treatment and the effect of the radiation therapy while further reports showed that the results may not be so accurate due to the low sample size (26).

At two thousand fifteen, the association of the thyroid in America suggested a guideline of the thyroid tumor, according to them, this patients classified in to three types: those with low risk and those with intermediate hazard and finally a high risk patients and they decide to increase of intermediate one of recurrent of the tumor to more than nine percent while those of high risk there is a doubling of the percent to more than forty percent and most of these patients showed the elevated of the Tg level although they did not regard this marker as a diagnostic one and this may be due to that the sensitivity of the Tg test cannot diagnose the elevated level whether is due to normal unremoved tissue or tumor one although all those with high risk take the radiation therapy and this therapy improve the complete removal of tumor tissue and even survival aspect. Those with tumor size less than one centimeter regarded as low risk one and there is no need for post operative treatment. Those of tumor regarded as an intermediate may take the iodine therapy (27).

The difference of respond to the treatment was cleared by two studies which clarify the effect of the treatment on the level of assessment of the Tg. After intake of treatment postoperatively and these two studies revealed that those of Tg level less than 0.12 nanogram per milliliter with negative nodule indicated a perfect response and the chance of recurrence is rare. On the other hand, those with negative post operation nodule with Tg level more than one nano gram per milliliter are shoed an elevated chance of mortality. One obstacle on this research is the failure to diagnosis the malignant tumor from the benign one particularly in moderate degree tumor (28). The monitoring of theses tumor patient for a long time may during the incidence of the tumor and diring one year indicated that most of the observed cases of re-incidence of the tumor occurred during the first year, but some of them the recurrence if the tumor occur after two years (29). The managements is vary according to the year or re-incidence. This assessment is depend on the US,

Tg and TSH if it re-occurred during the first year. Those with high risk may even be revealed by CT scan and other interventions especially those who fail to respond to the treatment during the first year whether high or even intermediate risk patients. Radioactive assessment is preferred for those of high risk more than of low or intermediate risk. (30-32).

It is better to make the test every three or six months at the first year then every nine months to one year after two years as the chance of recurrence is severely reduced. With reduced level of the Tg and absence of the Abs, the good prognosis is more proven. Those with removal of only one lobe of the gland make the doctor face an obstacle due to that they cannot diagnose the Tg level whether it is the normal of malignant tissue and so the strategy of the treatment may be severely different from one doctor to another and even from one oncology centre to another, although it can be accurately diagnosed by aspiration from the remaining tissue with a cytology opinion and the culture revealed the results with continuous US for the neck every three to seven months in the first year and every nine months to even a year after two years (33-36).

## CONCLUSION

COVID and many other reasons is one of the main factors that could be ends with thyroid tumors and the Tg assessment alone may not be enough as a predictor for the thyroid carcinoma and may need further measurements and even for a regular intervals using different technique. The stages of the tumor depends on the speed of the surgical removal and even the need to the traditional therapy.

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