

The clinical utility and cost effectiveness of routine thyroid screening in adult psychiatric patients presenting at Stikland Hospital, Cape Town, South Africa

A Lachman¹, KJ Cloete¹, M Kidd², R Schoeman¹

¹Department of Psychiatry, University of Stellenbosch, Tygerberg, South Africa

²Centre for Statistical Consultation, University of Stellenbosch, Tygerberg, South Africa

Abstract

Objective: The use of thyroid tests to assess psychiatric patients remains debatable. Therefore, this study was conducted to examine the utility and cost effectiveness of the current protocol used in thyroid testing in adult psychiatric patients presenting at Stikland Hospital, Cape Town, South Africa. **Method:** This was a retrospective chart review conducted at Stikland Hospital between 1 January 2000 and 31 December 2005. The following data was recorded: demographic variables, clinical diagnoses at admission and discharge, number of days from admission to a thyroid test request, the reason for thyroid screening, number of thyroid tests, their yield and costs involved, as well as the action taken following an abnormal thyroid test result. **Results:** The mean age of patients ($n = 1080$: $n = 364$ male, $n = 716$ female) was 42.8 years ($SD \pm 16.6$). Pre-existing thyroid disease was documented in 70 (6%) of patients. Normal Thyroid Stimulating Hormone (TSH) test results significantly ($p = 0.0001$) increased, whilst abnormal TSH test results significantly ($p = 0.0001$) decreased from baseline to follow-up. Except for gender, the outcome of TSH screening was independent of demographic and clinical diagnoses. Only 16% of TSH tests yielded clinically significant results. **Conclusion:** The findings of this study do not support the early, routine screening for thyroid dysfunction in psychiatric patients at this facility. It is possible that thyroid screening may present with transient abnormalities of no particular clinical significance, and would therefore not be a cost effective practice.

Keywords: Psychiatry; Screening; Thyroid abnormality; Thyroid stimulating hormone

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Introduction

Research has shown that thyroid disease may contribute to or precipitate mental illness.¹ Hypothyroidism has been linked to depression, cognitive impairment, and psychosis, while hyperthyroidism has been linked to mania, anxiety, hyperactivity, and transient psychosis.² Thyroid abnormalities may also present in psychiatric patients that are post partum, elderly or have a concomitant physical illness.^{3,4,5}

Although thyroid dysfunction in psychiatric illness is

common, the exact mechanism underlying the link between thyroid abnormalities and mental illness is unclear. The correlation between a specific thyroid dysfunction (over or under active) and psychiatric diagnosis has also been inconsistent. Furthermore, thyroid abnormalities have an inhomogeneous distribution across psychiatric diagnoses and are mostly observed in patients with affective disorders or schizophrenia.^{1,6} Multiple studies have also shown that patients admitted for acute psychiatric care have a prevalence of thyroid dysfunction that is similar to the general population.^{7,8,9} Nevertheless, psychiatric clinicians may wish to screen for thyroid abnormalities to exclude thyroid dysfunction as aetiology for psychiatric symptoms or to monitor patients on drugs that affect the thyroid gland.

Clinicians use the Thyroid Stimulating Hormone (TSH) measurement as the gold standard when screening for thyroid

Correspondence

Dr KJ Cloete
Faculty of Health Sciences, Department of Psychiatry,
University of Stellenbosch
PO Box 19063, Tygerberg 7505, South Africa
email: kjc@sun.ac.za / kaboutercloete@gmail.com

disease.^{5,10} In most studies, the yield of abnormal thyroid test results however remains low. Psychiatric clinicians should be aware that thyroid test abnormalities do not always denote thyroid disease and that the proper interpretation of test results is dependent on a good basic understanding of thyroid physiology and the methodology of the test.¹¹

In general, screening for thyroid dysfunction in the assessment of psychiatric patients remains controversial.^{12,13} Bannister et al.¹⁴ noted that as many as 21.7% of routine thyroid test results of psychiatric patients were abnormal, whilst studies by White and Barraclough¹⁵ found as few as 3% of thyroid test results abnormal. Research has also shown that up to 50% of psychiatric patients may have spuriously abnormal thyroid test results.^{16,17} Leo et al.¹⁸ suggested that in adolescents in the acute phase of mental illness, abnormal thyroid test results might be transitory and require confirmation. Therefore, routine thyroid testing among adolescent psychiatric inpatients are unwarranted except in those who display physical signs or symptoms suggestive of thyroid disease. Furthermore, the TSH in acute psychiatric patients is generally either normal or high, suggesting central activation of the hypothalamic-pituitary-thyroid axis.^{16,17} In most instances, the thyroid test results spontaneously normalise within 2 weeks, and treatment directed toward the thyroid gland is not indicated.¹⁹

Although TSH screening of psychiatric patients seems questionable, the use of thyroid tests may be helpful to assess certain categories of patients.²⁰ These include patients admitted to specialised geriatric units, nutritionally deprived patients who fail to respond to supplementation, those with a family history of thyroid dysfunction, pre-senile dementia, and women over the age of 40 with mood disorders. Some government protocols (e.g. United Kingdom, Australia) also suggest early, routine thyroid screening of acute psychiatric admissions.^{21,22} Similarly, in South Africa, baseline TSH testing is done on acute psychiatric admissions at a government-funded psychiatric hospital, Stikland, in Cape Town, South Africa, as set out in the Stikland Hospital Special Investigations Protocol for 2000. This standard practice may result in unnecessary costs to both patients and the hospital. Within this context, the aim of this study was to investigate the utility and cost effectiveness of the current protocol used in thyroid testing in adult psychiatric patients presenting at Stikland Hospital.

Methods

A retrospective review of all thyroid tests requested by Stikland Hospital between 1 January 2000 and 31 December 2005 was conducted by a single, independent investigator. Approval for this research was obtained from the institutional review board of the University of Stellenbosch (N05/07/125). The study was conducted in accordance with the revised Declaration of Helsinki²³ and the Medical Research Ethical Guidelines on Human Research of the Department of Health, 2004.

Patient records were reviewed to determine demographics, i.e. age, gender, history of thyroid disease or comorbid medical illness, substance use, concurrent medication use, and other factors such as stressors that might have influenced thyroid hormone levels. In addition, available clinical information of all patients with requested TSH tests was recorded, whilst clinical diagnoses on admission and

discharge were coded according to criteria of the Diagnostic and Statistical Manual of Mental Disorders IV-TR.²⁴

Thyroid tests included the measurement of any or all of the following: TSH, Free Triiodothyronine (FT3), and Free Thyroxine (FT4). Serum levels of TSH, Free Triiodothyronine (FT3), and Free Thyroxine (FT4) were determined using a microparticle enzyme immunoassay (Abbott AxSYM, National Health Services Laboratory, Greenpoint). The assay used was unchanged for the time period of this study, whilst the Coefficient of Variance for each assay (inter and intra) was <11%, representing an acceptable level of variability. In addition, the tests were performed at the National Health Services Laboratory in Greenpoint, which is an accredited laboratory that takes part in regular external quality control programs. The total number of thyroid tests performed (as per clinician request), their yield, and the record of action taken following an abnormal result were also documented. In addition, the reason for the thyroid test request, the number of days from admission to when a thyroid test was requested, as well as the cost of thyroid testing were also recorded.

Data analyses were performed using Statistica software, version 8. For comparison of continuous measurements between different groups, one-way ANOVA was used. Relationships between categorical variables were tested using cross tabulation and the Chi-square test, whilst baseline and follow-up data were compared using the McNemar test. A 5% significance level was used for determining statistical significance of results.

Results

Of the 2226 cases screened, 1050 (47.2%) contained missing or incomplete clinical data. The final sample thus consisted of 1176 (52.8%) cases. Statistical analyses were repeated after exclusion of an additional 82 (7%) cases where thyroid tests were repeated (i.e. re-tested or repeated on the same admission) more than once. The results yielded no significant differences between these two groups.

Demographics

The mean age of patients ($n = 1080$) was 42.8 years ($SD \pm 16.6$). Of these patients, 364 (34%) were male and 716 (66%) female. Females were significantly ($p = 0.02$) older (43.7 ± 16.4 years) than males (41.2 ± 17.0 years).

Co-existing medical illnesses

Pre-existing thyroid disease was documented in 72 (7%) of patients. An auto-immune illness was documented in 49 (4%) of patients, a metabolic dysfunction (hypertension, diabetes, asthma, and other endocrine diseases) in 373 (34%) of patients, and a history of an infectious disease (tuberculosis or syphilis) in 106 (10%) of patients. Epilepsy occurred in 61 (6%), whilst a developmental or growth delay was documented in 38 (3%) of patients. Only 7 (1%) of patients were breast feeding, while 20 (2%) of patients were in the post partum period.

Substance use

The use of alcohol, cannabis, methamphetamine and other substances was analysed according to lifetime prevalence (sum of past and/or current use). In all of those who had a history of alcohol use, 293 (86%) reported current use. In patients who

confirmed a history of cannabis use, 152 (86%) were still using cannabis. Among those with a lifetime use of methamphetamine, 28 (97%) confirmed current use of the drug.

Recent medication use

Antidepressants were prescribed to 302 (28%) of patients, antipsychotic medications to 249 (23%) of patients, mood stabilizers to 140 (13%) of patients, and thyroid medication to only 49 (5%) of patients. The use of "other medications" (antihistamines, antihypertensives or analgesia) were reported by 399 (36%) of patients, whilst 22 (2%) of patients were on contraceptive medications.

Stressors

The main stressors documented on admission are documented in Table I.

Stressors	Number of Patients (n=1096)*
History of family conflict	657 (60%)
Work /financial	544 (50%)
Injury or illness	600 (55%)
Death or loss of significant person	158 (14%)
Admission to hospital as stressful	78 (7%)

*Although n=1096, not every patient had a documented stressor, and in some cases more than one stressor was recorded for a single patient.

Clinical diagnoses

The most common primary diagnoses were major depressive disorder (n = 299, 28%) and psychotic disorders (n = 303, 28%). Bipolar disorder (mania) occurred in 197 (18%) of patients, dementia in 78 (7%) of patients, whilst anxiety disorders accounted for 38 (4%). Substance related (use and abuse) disorders made up 114 (11%), while 42 (4%) were documented as "other diagnoses" (e.g. adjustment disorders, or conditions due to a general medical condition).

Patients with dementia were significantly (p < 0.01) older (mean age ± SD: 70.4 ± 10.5) than patients with other documented diagnoses (Table II). Patients with psychotic disorder were also significantly (p < 0.05) older (mean age ±

	Number of patients	Mean Age	Standard Deviation
TOTAL	1071	42.8	16.6
Depression a	299	40.2	14.5
Psychosis b	303	42.7	15.8
Dementia d	78	70.4	10.5
Anxiety ac	38	37.4	15.5
Substances c	114	35.8	12.6
Other ab	42	42.1	14.7
Bipolar/Mania ab	197	41.5	15.0

Different superscript letters represent significant (p < 0.05) differences between diagnoses in terms of age.

SD: 42.7 ± 15.8) than patients with anxiety disorders (mean age ± SD: 37.4 ± 15.5), substance use (mean age ± SD: 35.8 ± 12.6), and depression (mean age ± SD: 40.2 ± 14.5) (Table II). Depression was found to occur more commonly in females, while substance use was more prevalent in males (p < 0.01).

Day of thyroid test request

The mean number of days from admission to when a thyroid test was requested, excluding outliers, was 6.7 ± (12.69) days. Outliers (range 0 -140) included extended admissions, chronic long-term patients, or where thyroid tests were conducted as follow-up of previous results. The median duration since admission was 3.0 days.

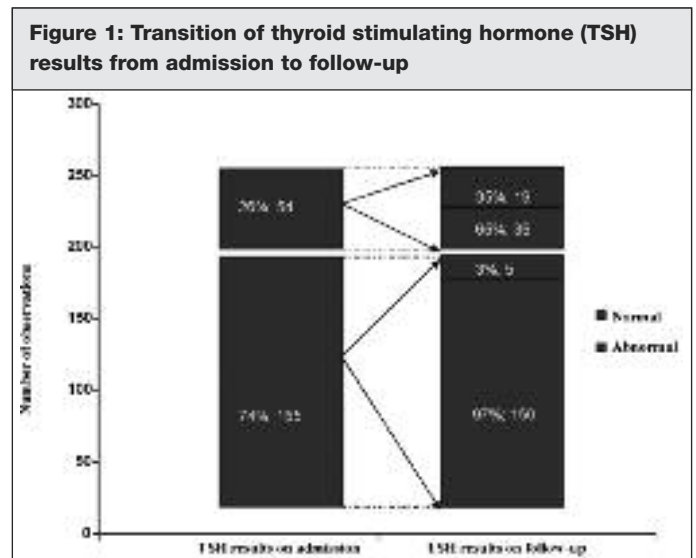
Reason for thyroid test request

Thyroid tests were routinely requested in 797 (73%) of patients, while 402 (37%) thyroid tests were requested based on clinical suspicion. Only 70 (6%) were known to have thyroid disease, whilst in 28 (3%) screening was requested due to treatment non- response. No thyroid tests were requested in the case of a family history of thyroid dysfunction.

Thyroid test results

Only 209 records contained complete baseline and follow-up thyroid test results. Most of the TSH tests done at baseline (n = 155) and follow-up (n = 150) yielded normal results, whilst a small proportion (n = 5) yielded abnormal results at follow-up (Figure 1). The TSH tests that yielded abnormal results at baseline (n = 54) decreased at follow-up (n = 19), whilst the majority (n = 35) normalized at follow-up (Figure I). The number of normal results increased significantly (p = 0.0001) from baseline (n = 155) to follow-up (n = 185). In contrast, abnormal test results showed a significant (p = 0.0001) decrease from baseline (n = 54) to follow-up (n = 24).

There were significantly (p = 0.013) more abnormal results amongst female patients 121 (17%) than amongst male patients 41 (11%). However, this was not clinically significant. The outcome of TSH test results in this sample was also independent of admission diagnoses. Furthermore, no relationship was demonstrated between abnormal thyroid test results and the presence of stressors, medication use, co-existing medical illnesses, or substance abuse in the sample.



Cost of TSH testing

The costs per test are summarized in Table III. There were 1093 test requests for TSH, whilst T3 (n=111) and T4 (n=112) tests were also requested. As mentioned earlier in the text, only 209 of the 1093 TSH tests requested on admission had complete records in terms of admission and follow-up TSH test results. No TSH follow-up test results were reported in 471 of the 1093 cases, whilst 411 were discharged to local clinics and 2 referred to endocrinology. These cases were excluded, whilst any file with a repeated request was also excluded from the analyses.

Table III: Costs of thyroid tests

	TSH ^a	T3 ^b	T4 ^c
Number of tests	1093	111	112
Cost per test	R120.50	R107.50	R53.75
Total cost of tests	R131 707	R11 933	R6020

^aThyroid Stimulating Hormone; ^bTriiodothyronine; ^cThyroxine

Cost utility of abnormal results

Of the 162 abnormal results on admission, 35 became normal on follow-up, 19 remained abnormal, and 108 had no recorded action or were discharged (Figure 1). The cost of transition of the 35 abnormal results to a normal result was R4217.50. Similarly, the cost of the undocumented 108 results on follow-up amounted to R13 014.

Cost utility of the normal results

Of the 931 normal results on admission, 150 remained normal, whilst 5 became abnormal on follow-up (Figure 1). For 776 originally normal results, there was either no recorded action on follow-up or patients were discharged without follow-up. The cost of these 776 results amounted to R93 508.

Overall cost utility

The cost of TSH testing amounted to R131 706.50. The cost of doing tests for which follow-ups were not documented, results were unknown, patients discharged, or resulted in transitions to normal results amounted to R1 10 739.50. The utility therefore amounted to R20 967, which was only 16% of all TSH tests done.

Discussion

To our knowledge, this is the first documented analyses of the clinical utility and cost effectiveness of the routine practice of thyroid screening in a South African inpatient psychiatric population. It was found that thyroid tests were requested in 2226 patients presenting to Stikland Hospital. However, due to inadequate record keeping or missing files, analyses of only 52.8% of this sample was possible. In 73% of the sample population, thyroid tests were requested "routinely" i.e. without any clear indication of the clinical reason, documented previous history or family history of thyroid disease. Only in 37% of cases, clinical suspicion was reported as a reason for requesting thyroid screening.

The ordering of routine thyroid tests at Stikland hospital

for this study period appeared to be performed as per protocol, despite findings from a local study done in 2000 at the same Hospital.²⁵ This study documented that new psychiatric patients were subjected to unnecessary, costly and unhelpful special investigations, and recommended that the only "routine" screening that should be performed on these patients, was that for syphilis. In other reports, it was also pointed out an excess number of laboratory procedures are needlessly requested to assess psychiatric patients.^{26,27}

To assess psychiatric patients at this facility, thyroid tests were requested in a short period after admission, with a median of 3 days. This practice of early thyroid screening is not consistent with recommendations in literature.^{26,19,18} Patients hospitalised for psychiatric reasons may experience transient increases in thyroid indices secondary to the stress of hospitalisation.²⁸ In most cases, these spurious thyroid abnormalities may spontaneously normalise within 2 weeks. Therefore, it was suggested that thyroid screening be done at least one week after admission.¹⁹

Interestingly, no significant relationship was found between the presence of an abnormal TSH test result and co-existing medical conditions, documented stressors, or medication use. However, a critical review by Baumgartner²⁹ suggested that abnormal thyroid hormone values are due to intervening variables such as physical illness, psychotropic medications or multi-factorial stressors. In this sample, it was not possible to assess the true impact of these factors, since this was a retrospective study where we were unable to verify patient compliance on medication or comment on the extent of stressors. Another possible explanation for the lack of impact of the documented illnesses and stressors on the TSH could be the presence of "Euthyroid Sick Syndrome". In this condition, a state of dysregulation of thyrotropic feedback control may occur, where the levels of T3 and/or T4 are at unusual levels, but the thyroid gland itself (measured by the TSH) does not appear to be dysfunctional. This is often seen in critical illness, severe stress or in starvation, and may have been the case in some of our patients. However, due to the fact that T3 and T4 were not requested in all of the patients, we are unable to offer further comment on this possibility.

No associations were also demonstrated between abnormal test results and a history of substance use, i.e. alcohol, cannabis or methamphetamine. This contradicts findings by Morley and Schafer³⁰, who reported abnormal baseline thyroid functions in patients with a history of substance abuse, particularly alcohol abuse, and admitted to psychiatric hospitals. A direct toxic effect of alcohol upon thyroid function has also been suggested in men suffering from alcoholism and exhibiting a reduction in thyroid gland volume.³¹

The study also surprisingly found no statistically significant relationships between the type of diagnosis and abnormal test results. In contrast, studies have shown that patients with thyroid abnormalities may be depressed^{32,33}, may present with cognitive dysfunction¹⁵ or with psychosis.³⁴ We also specifically found no significant relationships between a feature of mood or the type of

mood disorder and an abnormal test result. This is similar to previous studies, which found that while frank hypothyroidism can precipitate depression, most depressed patients are clinically euthyroid.^{32,35} Furthermore, no association was found between a diagnosis of dementia and an abnormal thyroid test result. This contradicts numerous studies that report an increased prevalence of thyroid dysfunction in the elderly inpatient population.^{36,3,37}

Of the 1096 records that were suitable for statistical analysis, only 209 records of thyroid test requests contained complete information regarding action on follow-up of routine thyroid tests requested. Price³⁸ suggested that only when appropriate action is taken on follow-up, would any test be beneficial. Of the 162 originally abnormal test results, only 12% remained abnormal, whilst the rest either normalised (indicating false positives) on repeat testing or were not followed up, therefore questioning the clinical utility of the initial routine testing. Sackett³⁹ also suggested that the practice of routine thyroid screening may result in "false positive" results and lead to unnecessary expensive and intrusive follow-up tests. As suggested previously, the transient nature of abnormal thyroid test results may be a reflection of a multitude of factors, which include the timing of testing, the stress response, influence of comorbid physical conditions, concurrent substance and/or medication use or differences in physiological responses in the patient population.²⁸

Limitations

This study was a retrospective chart audit and it was therefore not possible to determine the accuracy with which the admission diagnoses were recorded. Other reasons for requesting screening, besides physical, were not always documented in the notes and as a result could not be verified. In addition, Quality of Life Measures were not considered due to the retrospective nature of the review. Ideally, a prospective study would consider a more comprehensive means of establishing cost-effective practice in the setting of Quality of Life years. A prospective study would in addition assist one in determining which particular groups of psychiatric patients should ideally receive TSH screening on admission and follow up.

Conclusion

In our sample, we demonstrated an overall clinical utility of thyroid testing in psychiatric patients of only 16%. Of the overall cost, 84% resulted in a wastage of scarce resources, since screening were either performed without a clear follow-up action or too early where chances of spurious abnormalities were greater. Overall, our findings do not support the early, routine screening for thyroid dysfunction in all psychiatric admissions, since screening is likely to present with transient abnormalities of no particular clinical significance, and would therefore not be a cost effective practice. Other studies have also questioned the rationale and clinical utility of routine thyroid screening of newly admitted psychiatric patients.^{40,41,18} Generally, TSH testing in psychiatric patients should be guided by relevant clinical history and physical findings and these should be adequately documented in clinical case notes. We recommend that in keeping with international guidelines,

"routine testing" of thyroid should be limited to those in particular high risk categories, including women >45 yrs, geriatrics, those with known history of thyroid abnormalities, and those with serious comorbid medical illnesses. In a resource restrained health service, patient outcomes and management may be better served by directing resources towards higher yielding interventions.

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