

Incidence Of Hypoparathyroidism After Total Thyroidectomy for Benign Goitres. A Systematic Review

Muhammad Tahir Ghani¹, Hafiz Muhammad Ijaz ul Haq², Ibad Ur Rehman³, Huma Azam Malik⁴

Abstract

Objective: systematic review assessed the overall incidence of hypoparathyroidism after Total thyroidectomy (TT) for benign goitres.

Methods: A systematic search of PubMed, google scholar, Cochrane, and Pakmedinet under PRISMA (preferred reporting items for systematic reviews and Meta-analyses) guidelines was performed. All studies during the last 50 years where TT was performed for benign goitres and post-operative hypoparathyroidism was assessed were included. The total incidence of both transient and permanent hypoparathyroidism was calculated after TT for benign goitres. The risk of bias was also assessed.

Results: Twelve studies were included in total including eight retrospective, three prospective observational studies, and one randomized trial. Three studies were from Turkey, 2 from Pakistan, 2 from Greece, and one each from Saudi Arabia, India, Denmark, Egypt, and the USA. 2809 TT were performed for benign goitres. Overall Transient hypoparathyroidism (THP) was noted in 290 (10%) patients while permanent hypoparathyroidism (PHP) was noted in 33(1.17%) patients. The highest incidence of permanent hypoparathyroidism was 17% in one study while the lowest was 0% in three studies. The highest incidence of transient hypoparathyroidism was 28.5% in one study while the lowest incidence was 2.5%. The risk of bias was high.

Conclusion: TT for benign goitres is associated with 1.17 % overall risk (range 0%-17%) of PHP and 10% (range 2.5%-28.5%) of THP.

Keywords: Total thyroidectomy (TT), Benign goitre, Transient hypoparathyroidism (THP), Permanent hypoparathyroidism (PHP).

¹ Surgery Surgical Specialist, Aero Hospital, Hassan Abdal; ² Assistant Professor, Akbar Niazi Teaching Hospital, Islamabad; ³ Senior Registrar, Akbar Niazi Teaching Hospital, Islamabad; ⁴ Senior Registrar, Akbar Niazi Teaching Hospital, Islamabad; ⁵ Surgery Surgical Specialist, Aero Hospital, Hassan Abdal

Correspondence: Dr Muhammad Tahir Ghani, Surgery Surgical Specialist, Aero Hospital, Hassan Abdal. **Email:** doctortahir226@gmail.com

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1. Introduction

While total thyroidectomy (TT) for differentiated thyroid carcinoma is considered the preferred treatment¹, the ideal surgical treatment for benign goitres is still a matter of debate². Total, near total, and subtotal thyroidectomies, are performed for bilateral benign goitres^{2,3,7}. Until the end of the 20th century, subtotal thyroidectomy (STT) was considered the best option for benign goitres⁴ however there is a gradual shift towards TT for benign bilateral goitres. In the Western world, the trends are more towards TT for benign goitre⁴, while in the developing world still TT for benign goitre is a matter of concern⁵ due to the assumed higher rate of complications^{2,3}.

Usually, the patients having benign goitres are managed conservatively and the indications for surgery include pressure symptoms, suspicion of malignancy, cosmetic concerns of the patient, and hyperthyroidism^{2,6}. The greatest disadvantage of subtotal or near-total thyroidectomy is goitre recurrence in spite of pharmacological thyroid

suppression post-operatively^{2,7}. Surgery for recurrent goitre carries a significantly high risk of recurrent laryngeal nerve injury and hypoparathyroidism^{2,3,7,8}. TT which involves the complete removal of the whole thyroid gland carries a potential risk of recurrent laryngeal nerve injury and damage to parathyroid glands leading to temporary or permanent hypoparathyroidism although eliminating the risk of goitre recurrence^{3,5,9}.

The reported incidence of hypoparathyroidism after TT for benign goitre is variable. Some studies document THP incidence as high as 30-50 %¹⁰. PHP according to many is defined as failure of the parathyroid glands to regain normal function after 6 months post thyroidectomy^{11,12} while few consider it as permanent after 01 years of surgery¹³. Some studies report the incidence of PHP after TT as low as zero percent^{14,20,22}, while few report incidence of PHP after TT as high as 17 %⁹. This difference may be associated with many factors like lack of expertise of surgeons, lack of specialized endocrine surgeons, size of goitres, and hyperthyroidism.

The aim of this systematic review is to gather all existing knowledge about post-TT hypoparathyroidism around the globe and to find out the incidence of transient and PHP after TT for benign goitres. This will help surgeons to adopt a uniform policy of TT for benign goitres.

2. Materials & Methods

This systematic review was conducted as per PRISMA (preferred reporting items for systematic reviews and Meta-analyses) guidelines¹⁵.

Search strategy:

PubMed, google scholar, Cochrane, and Pakmedinet were searched on 29th September 2022. The following keywords were used for each database. Total thyroidectomy, parathyroid gland injury, post-thyroidectomy hypoparathyroidism, simple multinodular goitre, benign goitre, and post-thyroidectomy hypocalcemia. All retrospective, prospective studies, clinical trials, and randomized clinical trials were included. The search was limited to studies published in the English language during the last 50 years to see recent trends.

Inclusion criteria: All cases of TT done during the last fifty years for benign conditions in adults above 18 years, where post-surgery hypoparathyroidism was recorded, manifested either clinically or biochemically were included. Permanent hypoparathyroidism (PHP) was defined as symptomatic hypocalcemia or undetectable Parathyroid hormone biochemically after 06 months of surgery. All studies in which a comparison of various surgical options for benign goitres was done were also included. Only freely available full-text studies are included.

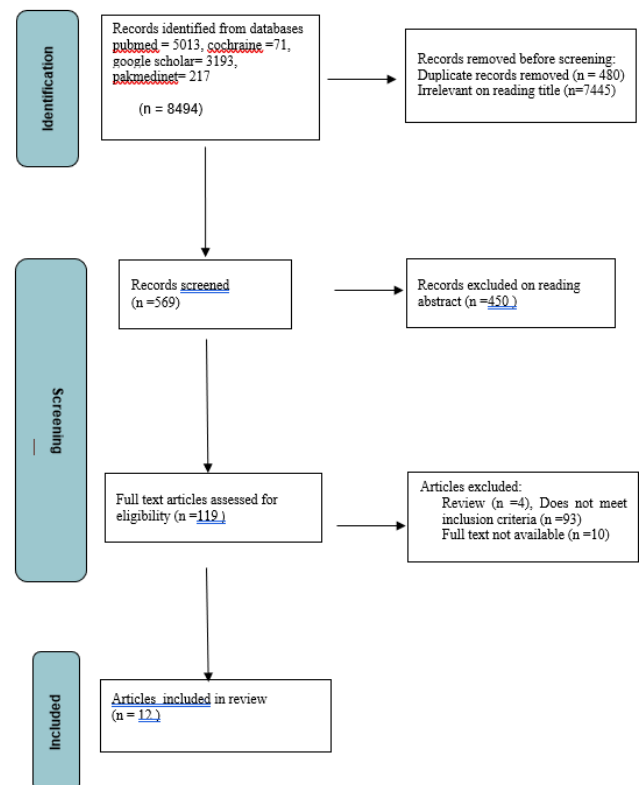
Exclusion criteria: Total thyroidectomies performed for malignant conditions, or recurrent thyroids and completion thyroidectomies were excluded. Studies, where post-TT hypoparathyroidism for benign conditions was not separately recorded from malignant conditions, were excluded as well. Lobectomies were excluded as well.

Risk of bias assessment:

All observational studies were analyzed for risk of bias as per Newcastle - Ottawa quality assessment scale for observational studies²⁴. None of the studies got the highest stars i.e., 9 and all observational studies remained between five and three stars. One randomized

control trial by Sewefy et al²¹ was analyzed by the Cochrane Risk of Bias tool for randomized studies²⁵ and had a high risk of bias as the blinding of participants and personnel was not specified (performance bias).

Prisma flow diagram



3. Results

Twelve studies were included in this systematic review. Eight were retrospective and three were prospective observational studies and one was a randomized control trial. Three studies were conducted in Turkey, two in Pakistan, and two in Greece, while one study was conducted in the USA, India, Denmark, Egypt, and Saudi. A total of 2809 total thyroidectomies were performed for benign goitres. 2008 (71%) were females in eleven studies, while one study ozbas et al¹⁸ did not record female patients separately. In six studies thyroidectomies were performed by general surgeons while by endocrine surgeons and ENT surgeons in one study each. Four studies didn't mention the speciality of surgeons performing thyroidectomies.

Summary of the studies included in a systematic review

Reference	country	Study design	No of TT'S	Female gender	Follow up
Alharbi f et al ¹⁶	Saudi Arabia	Retrospective study	320	208(65%)	Self reporting
Latif s et al ¹⁷	Pakistan	Retrospective study	96	78 (81.2 %)	self reporting
Ozbas s et al ¹⁸	Turkey	Retrospective study	260	NR	18 months
Vassiliou I et al ¹⁴	Greece	Retrospective study	116	82(70 %)	self reporting
Ciftci f et al ⁷	Turkey	Retrospective study	258	205(79%)	self reporting
Efremidou EI et al ¹⁹	Greece	Retrospective study	900	738 (82%)	self reporting
Gangappa rb et al ²	India	prospective			
		Randomized study	116	101(87%)	06 months
Jensen pv et al ⁹	Denmark	Retrospective study	114	99(86.8%)	13 months
Koyuncu a et al ²⁰	Turkey	Prospective study	58	42(72%)	02 years
Sewefy am et al ²¹	Egypt	prospective RCT	112	92(82%)	03 years
Lodhi mf et al ²²	Pakistan	prospective study	196	147(75%)	06 months
Bauer ps et al ²³	USA	Retrospective study	263	216(82%)	06 months

*TT: Total thyroidectomy, NR: not reported, RCT: Randomized control trial

Transient hypoparathyroidism (THP) manifested by symptomatic hypocalcemia was noted in 10% (290) of patients. The highest incidence of THP was 28.5%, noted in a study conducted by Lodhi MF et al²² in Pakistan. The lowest incidence of THP 2.5% was noted in a study conducted by Alharbi f et al¹⁶ in Saudia. The range of THP was between 2.5% -28.5%.

Hypoparathyroidism was defined as permanent when hypocalcemia did not settle in 06-month time postoperatively. The overall incidence of permanent hypoparathyroidism (PHP) was 1.17% and was seen in 33 patients. The highest incidence of PHP was 17 % recorded in a retrospective study conducted by Jensen pv et al⁹ in Denmark. All these thyroidectomies were performed by ENT surgeons. The lowest incidence of PHP i.e. zero per cent was noted in three studies Vassiliou I et al¹⁴, Koyuncu et al²⁰, and Lodhi MF et al²² conducted in Greece, Turkey, and Pakistan respectively. The overall range of PHP was between 0%-17%.

Cont. Summary of the studies included in a systematic review

Reference	Primary surgeons	No of transient	No of permanent
		hypoparathyroidism	hypoparathyroidism
Alharbi f et al ¹⁶	NR	8(2.5%)	3(0.9%)
Latif s et al ¹⁷	NR	3(3.125%)	1(1.04%)
Ozbas et al ¹⁸	consultant surgeons	30(11.5%)	1(0.384%)
Vassiliou I et al ¹⁴	NR	7(6.03%)	0(0 %)
Ciftci f et al ⁷	experienced G. Surgeons	39 (15%)	1(0.38%)
Efremidou EI et al ¹⁹	Spec. endo surgeon	68(7.5%)	3(0.3%)
Gangappa rb et al ²	General Surgeons	19(16.37%)	1(0.86%)
Jensen pv et al⁹	ENT Surgeons	26 (22%)	20(17%)
Koyuncu a et al ²⁰	General Surgeons	14(24%)	0(0%)
Sewefy am et al ²¹	General Surgeons	13(11.6%)	1(0.89%)
Lodhi MF et al ²²	General Surgeons	56(28.5%)	0(0%)
Bauer ps et al ²³	NR	7(2.6%)	2(0.76%)
Total incidence of		290(10 %)	33(1.17%)
Hypoparathyroidism		Temporary	Permanent

*NR : not reported G.surgeons: General surgeons Spec.endo : specialized endocrine

5. Discussion

Surgical management of benign goitres is generally indicated once patients present with obstructive or pressure symptoms due to enlarging the size of the thyroid^{2,6,26}. Surgery is preferred for toxic goitres as well once toxicity is controlled with pharmacological treatment as the post-surgical management for hypothyroidism after total thyroidectomy is easy and straightforward in comparison to hyperthyroidism²⁷. TT eliminates the risk of goitre recurrence which is difficult to treat and surgery of recurrent thyroid is technically challenging and is associated with more post-op

morbidity in the form of recurrent laryngeal nerve injury and hypoparathyroidism^{2,7,28}.

In developing countries, thyroid surgeries are usually performed by general surgeons as specialized endocrine surgeons are not available²⁹ and this speciality is not born yet in our society. In our systematic review, TT was performed by specialized endocrine surgeons in only one study conducted by Efremidou EI et al¹⁹ in Greece. In six studies TT was performed by general surgeons, in one study by ENT surgeons while four studies didn't clearly mention the speciality of treating surgeons.

The main concern in avoiding TT in benign goitres is the risk of recurrent laryngeal nerve injury and hypoparathyroidism. The incidence of recurrent

laryngeal injury after TT is reported in the literature between 1.5-14%³⁰. We found in our review the overall incidence of permanent hypoparathyroidism (PHP) after TT for benign goitres was 1.17% (range 0-17%). The highest incidence of PHP was found in a study conducted by Jensen *et al*⁹ in Denmark. All cases of TT in this study were done by ENT surgeons. Lack of proper surgical training may be an important cause of the high incidence of hypoparathyroidism after TT. The highest incidence of PHP *i.e.* 17% was noted in a single study. The rest of the studies (excluding Jensen *et al*⁹) report very low incidence and the range of PHP drops down between 0% - 1.04% in the rest of the studies. The overall incidence of transient hypoparathyroidism (THP) was found in our review as 10% (range 2.5%-28.5%). The highest incidence was noted in a study conducted by Lodhi MF *et al*²² in Pakistan *i.e.* 28.5%. THP leads to prolonged hospital stay post-surgery but the majority of cases settle down in less than 06 months time.

We have found in this systematic review that total thyroidectomy for benign goitres is now a widely practised and adopted surgical procedure in both developed and developing countries. We found two studies of Pakistan and one study of India^{2,17,22} where TT for benign goitre was done with acceptable and comparable rates of post-op hypoparathyroidism. Benign Goitre is more common in females due to more prevalence of iodine deficiency in women of childbearing age³¹ as is evident in our review. 71% of patients undergoing TT for benign goitres were females reported in 11 studies.

5. Conclusion

TT is associated with a 1.17% overall risk (range 0%-17%) of permanent hypoparathyroidism and a 10% (range 2.5%-28.5%) risk of transient hypoparathyroidism and is a safe and preferred surgical option for benign goitres.

CONFLICTS OF INTEREST- None

Potential competing interests: None to report

Contributions:

M.T.G - Conception of study

M.T.G - Experimentation/Study conduction

M.T.G, H.M.I.U.H, I.U.R -

Analysis/Interpretation/Discussion

M.T.G - Manuscript Writing

M.T.G, H.M.I.U.H - Critical Review

M.T.G, H.M.I.U.H, I.U.R, H.A.M - Facilitation and Material analysis

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