Effects of Physical Activity on Thyroid Stimulating Hormone Levels in Obese Metabolic Syndrome Patients: A Meta-Analysis

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ABSTRACT

Metabolic syndrome is a combination of multiple disorders that predispose an individual to risk of diabetes, obesity, cardiovascular diseases (CVDs), cerebrovascular accidents (CVAs), and insulin-resistance. Hypothyroidism is the most prevalent metabolic disorder causing obesity, followed by hypercortisolism and hypogonadism. Hence, this study aimed to determine the effects of various exercises on thyroid stimulating hormone (TSH) levels in obese patients with metabolic syndrome. The study conformed to the preferred reporting items for systematic reviews and meta-analysis (PRISMA) standards. The PubMed, Cochrane, Google Scholar, Medline, and Biomed Central databases were searched using the keywords exercise, aerobic, rehabilitation, etabolic syndrome, and thyroid stimulating hormone. Studies in English language published between 2010 and 2021 and that examined the efficacy of physical therapy management with sham treatment on TSH levels in patients with obesity were included. The meta-analysis comprised of 526 patients with metabolic obesity from 10 randomised controlled trials. The analysis revealed that when compared with the control group, exercise had a moderate pooled effect on lowering TSH levels, with an effect size standardised mean difference (SMD) of -0.56 (95% Confidence Interval (CI), -1.09−0.02) estimated using a random effects model, with an I^2 of 86.61% (95% CI, 77.31–92.10) in the interventional group. It was concluded that although a pooled moderate effect of training on TSH levels was observed when all the studies were analysed using a continuous measure analysis SMD model, an individual analysis of the studies revealed a mild effect, with many studies also revealing the negative impact of training on TSH levels. Nonetheless, exercise-based intervention strategies are safe and effective as a management strategy for hypothyroidism and obesity due to hypothyroidism.

Key Words: *Thyroid hormone, Exercise, Metabolic syndrome, Obesity, TSH level*.

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INTRODUCTION

According to the National Health and Nutrition Examination Survey, the prevalence of metabolic syndrome in adolescents and adults is rapidly increasing.[1] In Pakistan, over the last few decades, 18–46% of the population had metabolic risk factors, as compared to other South Asian countries.[2] Metabolic syndrome is a combination of multiple disorders that predispose an individual to the risk of diabetes, cardiovascular diseases (CVDs), cerebrovascular accidents (CVAs), and insulin-resistance.[1] In addition, endocrine disorders are the leading cause of obesity. The most common endocrine condition is hypothyroidism, which accounts for 58.3% of all cases—followed by hypercortisolism (9.3%) and hypogonadism (22.3%)—making hypothyroidism the primary source of endocrine causes of obesity.[3]

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Furthermore, obesity, along with insulin-resistance, has increased the risk of Type-2 diabetes mellitus, leading to a vicious cycle of metabolic syndrome.[4] The root cause of metabolic dysregulation in the sexes is strongly associated with obesity.[5] According to the World Health Organization, the incidence of obesity is rising, with 57.8% of adults globally predicted to be considered obese by 2030. Obesity is an abnormal buildup of body fat that leads to health problems, including cancer.[6] Therefore, obesity is a critical public health issue that should be addressed to avoid obesity-related health complications.[7] According to a study conducted in 2015, obesity has become a global public health concern that has impacted the rates of morbidity and mortality, along with the cost of health care.[8] However, the development of these diseases is not only intrinsically dependent on obesity, but also on the presence of the fat mass and obesity-associated (FTO) gene.[9,10] The genome-wide association study (GWAS) analysis, which involved multiracial populations, has documented the association between FTO gene and the risk of various types of cancers and obesity.[10]

Over the last three decades, there had been an exponential growth in the prevalence of obesity; incidences of this condition nearly doubled among the adult and childhood population and tripled among adolescents. This had led to healthcare practitioners and policymakers devising strategies to manage the menace of worldwide diseases.[8] Owing to the increasing risk of obesity, all individuals, irrespective of age, gender, and demographic characteristics, are now susceptible to this condition. Hence, researchers are shifting their focus from devising preventive strategies to treatment approaches for obesity.[11] Several guidelines from the Obesity Society had been prepared to guide healthcare professionals in treating obesity; they outlined multiple therapies, such as lifestyle modifications, increased physical activities, dietary changes, and medications.[12]

Surgery is recommended in some cases. Several pieces of literature related to the effects of exercise in managing obesity are available. In these reports, aerobic or resistance exercises or combinations of conditioning forms are emphasised. However, to the best of the authors' knowledge, to date, no studies have evaluated the exercise dose and associated response.[13] The study aimed to determine the effects of different exercises on thyroid stimulating hormone (TSH) levels among patients with obesity.

The PubMed, Cochrane, Google Scholar, Medline, and Biomed Central databases were searched using the keywords exercise, aerobic, rehabilitation, metabolic syndrome, and thyroid stimulating hormone, to obtain studies on the effect of exercise on TSH. The inclusion criteria was studies published in English between 2010 and 2021 that examined the efficacy of physical therapy management with a sham treatment on TSH levels in patients with obesity. Trials without a control group or condition and participants with comorbidities were excluded. Studies for which full-text articles were unavailable or those that were published in a non-preferred language were excluded. Obesity was defined as BMI > 30 kg/m^2. Physical activity included aerobics, resistance training, and yoga.

Data abstraction and quality evaluation were performed using the inclusion and exclusion criteria under a uniform methodology. A data mining form was designed by extracting study information, such as author's name, publication year, targeted population, and treatment duration (Table I). This study followed the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines.

The risk of bias for random allocation, allocation concealment, blinding of participants and outcome assessors, insufficient outcome data, and selective reporting was evaluated using the Cochrane tool.[14]

Data were examined using MedCalc statistical software, version 18.11.3. In a random-effects model, the pooled impact was calculated using the continuous measurement standardised mean difference (SMD) method (I^2 at 95% CI). The data were evaluated using Hedges' *g* statistics, SMD tables, and forest plots. The findings were interpreted using Cohen's rule of thumb, which stipulated that values of 0.2, 0.5, and 0.8 indicated low, medium, and large effects, respectively. Cochrane's Q statistic and the percentage of heterogeneity were used to determine the level of heterogeneity. I^2 was calculated by dividing the number by Cochrane's Q value and removing the degrees of freedom (Df) to obtain a percentage value (I^2 = Q-Df/Q) of 0–100% (p<0.05), where 0% denoted no heterogeneity between the studies and higher values denoted a higher degree of variability.

RESULTS

A total of 7230 articles were retrieved in the initial searching through six database searches. Nine hundred and thirty original articles were evaluated based on their titles and contents. The relevant full-text articles were sorted and selected after screening of abstract, n=526 and finally, n=10 studies met the inclusion criteria to be included in the study. The flowchart of study inclusion is illustrated in Figure 1.

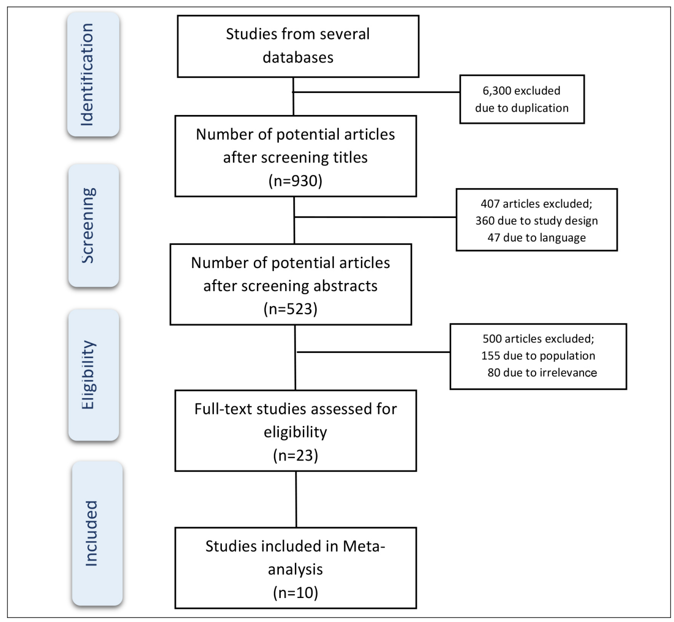

Figure 1: PRISMA flowchart of studies.

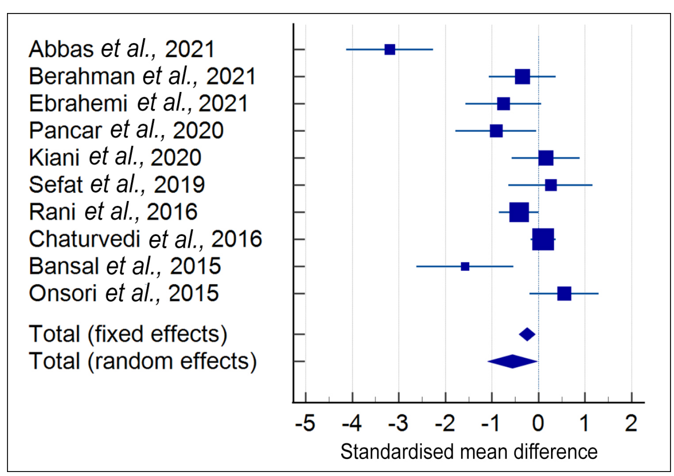

Figure 2: Forest plot of continuous measure standardised mean difference (SMD) for determining effect size.

Table I: Features of the included studies.

Author	Design	Age	Target Population	Groups	Intervention	Outcome Measures
Abbas *et al*., 2021[15]	RCT	20–35 years	Pregnant women with hypothyroidism	EG (n=21) CG (n=21)	EG: The treadmill-training programme was performed for 3 sessions/week i.e. one every other day for 12 weeks along with thyroxine replacement doses (100 µg/day). CG: The control group received thyroxine replacement doses (100 µg/day).	TSH
Berahman *et al*., 2021[16]	RCT	65–75 years	Post-menopausal women with metabolic syndrome	EG (n=16) CG (n=15)	EG: The 12-week training programme consisted of intermittent 60-minute water-based rhythmic exercise training 3 times/week. CG: Thyroxine treatment was administered to the control group	TSH
Ebrahemi *et al*., 2021[17]	RCT	45–55 years	Overweight men	EG (n=13) CG (n=13)	EG: Participants in the Pilates group performed Pilates training for 60–75 min, 3 times/week for 8 weeks CG: No intervention	TSH
Pancar *et al*., 2020[18]	RCT	20–22 years	Healthy individuals	EG (n=12) CG (n=12)	EG: A 6-week programme consisting of seven basic movements, including core strength exercises was provided to the participants. Exercise frequency was determined as 3 days/week. CG: No exercise	TSH
Kiani *et al*., 2020[19]	RCT	11–17 years	Inactive girls	EG (n=15) CG (n=15)	EG: Participants performed four weeks of moderate aerobic training, with 3 sessions/week at 70% maximal heart rate. CG: No exercise	TSH
Sefat *et al*., 2019[20]	RCT	8–15 years	Overweight girls with hypothyroidism	EG (n=10) CG (n=10)	EG: The experimental group performed weight training (40–65% of 1 RM) and aerobic exercise concurrently for 8 weeks. CG: The aerobic training programme consisted of 30-minute sessions that began at 60–70% heart rate reserve.	TSH
Rani *et al*., 2016[21]	RCT	18–45 years	Women with menstrual disorders	EG (n=45) CG (n=42)	EG: For a period of 6 months, participants received yoga intervention and medication. CG: Given prescribed medication	TSH
Chaturvedi *et al*., 2016[22]	RCT	40–60 years	Perimenopausal women	EG (n=111) CG (n=105)	EG: Participants received Hatha yoga; 21 poses were performed. The duration of intervention was 45-minute every day for 12 weeks. CG: Seven functional exercises were performed for a duration of 12 weeks.	TSH
Bansal *et al*., 2015[23]	RCT	30–40 years	Patients with hypothyroidism	EG (n=10) CG (n=10)	EG: The regular activity sessions were provided in the form of sports or running. All of the participants were stable on their respective thyroxine replacement doses (eltroxine) for 6 months. CG: Patients had maintained their respective thyroxine replacement doses (eltroxine) for 6 months.	TSH
Onsori *et al*., 2015[24]	RCT	40 years or above	Sedentary women	EG (n=15) CG (n=15)	EG: The training programme consisted of 12 weeks of moderate-intensity aerobic exercises with music, with three 60-minute sessions/week. CG: All participants were stable on their respective thyroxine replacement doses.	TSH

CG = Control group, EG = Experimental group, TSH = Thyroid stimulating hormone, RCT = Randomised controlled trial, RM = Repetition maximum.

Table II: SMD on random-effects model within 95% of CI and statistical heterogeneity.

Study	N1	N2	Total	SMD	SE	95% CI	t	p	Weight (%)	
									Fixed	Random
Abbas *et al*., 2021	21	21	42	-3.195	0.462	-4.128 to -2.262			3.73	9.05
Berahman *et al*., 2021	16	15	31	-0.345	0.353	-1.067 to 0.376			6.39	10.16
Ebrahemi *et al*., 2021	13	13	26	-0.751	0.394	-1.564 to 0.0618			5.12	9.75
Pancar *et al*., 2020	12	12	24	-0.913	0.416	-1.775 to -0.0514			4.60	9.53
Kiani *et al*., 2020	15	15	30	0.162	0.356	-0.567 to 0.891			6.27	10.12
Sefat *et al*., 2019	10	10	20	0.262	0.430	-0.642 to 1.166			4.29	9.38
Rani *et al*., 2016	45	42	87	-0.421	0.215	-0.848 to 0.00697			17.19	11.37
Chaturvedi *et al*., 2016	111	105	216	0.102	0.136	-0.165 to 0.370			43.13	11.88
Bansal *et al*., 2015	10	10	20	-1.582	0.496	-2.624 to -0.540			3.23	8.71
Onsori *et al*., 2015	15	15	30	0.557	0.362	-0.186 to 1.299			6.05	10.06
Total (fixed effects)	268	258	526	-0.246	0.0891	-0.421 to -0.0707	-2.757	.006	100.00	100.00
Total (random effects)	268	258	526	-0.561	0.272	-1.096 to -0.0261	-2.060	.040	100.00	100.00

Table III: Cochrane collaboration's tool for assessing risk of bias of included studies.

Author & Year	Random Sequence Generation	Allocation Concealment	Blinding of Participants and Personnel	Blinding of Outcome Assessment	Incomplete Outcome Data	Reporting Bias
Abbas *et al*., 2021[15]	+	+	?	?	+	+
Berahman *et al*., 2021[16]	+	+	?	?	+	+
Ebrahemi *et al*., 2021[17]	+	+	+	?	+	+
Pancar *et al*., 2020[18]	+	+	?	?	+	+
Kiani *et al*., 2020[19]	+	+	?	?	+	+
Sefat *et al*., 2019[20]	+	+	?	?	-	+
Rani *et al*., 2016[21]	+	+	+	+	+	+
Chaturvedi *et al*., 2016[22]	+	+	?	?	+	+
Bansal *et al*., 2015[23]	+	+	-	-	+	+
Onsori *et al*., 2015[24]	+	+	_	-	+	+

+ Low risk of bias, **-** *High risk of bias,* **?** *Unknown risk of bias.*

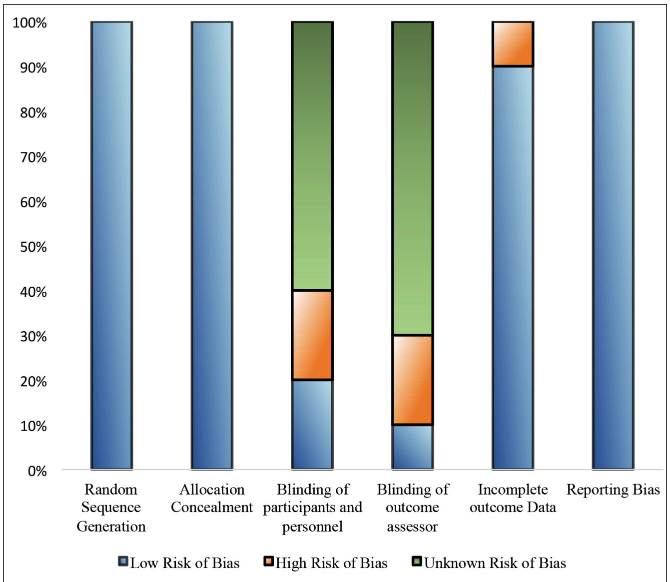

Figure 3: Cochrane risk of bias.

The results of 10 randomised controlled studies showed improved TSH levels in the physical therapy intervention group in comparison to the group that was only on medication or sham treatment. The effect size of physiotherapy intervention in terms of SMD in random-effects model indicated an impact of 0.56, which, per Cohen's rule of thumb, indicated that physical therapy management had a moderate effect on decreasing the TSH levels among individuals with obesity, as shown in Table II. The impact of physical therapy management was also examined using a forest plot, to reflect the pool effects in random-effects model at a 95% CI.

The level of inconsistency among the studies was 86.61 percent. Thus, the random-effects model was used to evaluate the pool effects. The percentage of heterogeneity among the SMD of the included studies was determined using the I^2 test and Cochrane's Q. With an effect size (SMD) of -0.56 (95% CI: -1.09 – 0.02) calculated using a random-effects model (I^2 of 86.61%), aerobic exercise had a moderate overall effect on lowering individuals' TSH levels, according to SMD by Hedges' *g* statistics (95% CI, 77.31 – 92.10, Table II, Figure 2).

Risk of bias was evaluated by using the Cochrane tool in the following domains, as shown in Table III and Figure 3. All studies showed a low risk of bias as they followed a randomisation sequence.[15-24] All studies had concealed allocation of participants.[15-24] Two studies considered participant and personnel blinding;[17,21] two studies showed high risk of bias,[23,24] whereas six studies showed an unknown risk of bias.[15,16,18,19,20,22] Seven studies showed an unknown risk of bias,[15-22] one study showed a low risk of bias,[21] whereas two studies showed a high risk of bias.[23,24] One study showed high risk of bias,[20] while the remaining had a low risk of bias in this regard.[15-18,21-24] A low risk of reporting bias was demonstrated in all ten studies.[15-24]

DISCUSSION

The findings of this study revealed that based on random-effects model, physical training has a moderate effect in terms of reducing the levels of TSH in patients with hypothyroidism and obesity. The analysis yielded an effect size (ES) of -0.56, I^2 = 86.361%, suggesting that physical training was effective for managing obesity by affecting thyroid secretion. The studies included in this review reflected a mild pool effect ranging from as low as -0.34515 to as high as -3.19514. Six studies included in this analysis indicated that exercises had a positive effect on TSH level, when compared with strategies such as pharmacological management and sham approaches, whereas four studies reported that exercise-based intervention strategies were less effective in reducing TSH levels among healthy individuals and those with obesity or hypothyroidism. However, individual SMD analyses of these four studies revealed that the TSH level increased from 0.16 to 0.55 in the exercise group. Altaye *et al*. conducted a study among adolescent patients with intellectual disabilities and hypothyroidism that showed increased levels of triiodothyronine (T3), tetraiodothyronine (T4) and decreased levels of TSH after performing 16 weeks of moderate intensity aerobic exercises.[25]

Similarly, in one study that evaluated the effects of acute aerobic exercise using a cycled ergometer on TSH levels in patients with hypothyroidism, the serum TSH levels were observed to be significantly reduced among the participants.[26] Another study involving university students aimed to determine the effects of a combination of aerobic and resistance training exercises. Herein, in the aerobic training-alone and control groups, 10 weeks of training, performed 4 days each week at an intensity of 45–55% for 30 minutes, significantly lowered the levels of TSH (p <.005) among sedentary males, whereas in the combined group, which included the same aerobic protocol with the addition of push-ups, sit-ups, and planks for 10 minutes, was also significantly effective (p <0.005) in affecting TSH levels. Interestingly, the training effects were similar in the combination and aerobic training groups, indicating that adding a different form of exercise did not result in greater reductions in TSH levels.[27] However, further multiple-centre studies involving larger sample should be performed to confirm the associated effects. The findings of our meta-analysis clearly demonstrated that exercise-based management approaches had a moderate effect in reducing TSH levels, and exercise-based interventional strategies should be incorporated as a distinct and adjunct approach to management in patients with hypothyroidism, particularly in those with obesity. In addition, studies incorporating the effects of exercise on T3 and T4 levels in association with TSH levels must be performed to further evaluate the effects of training on all thyroid gland biomarkers, to draw an association between thyroid biomarkers and physical training.

CONCLUSION

The analysis concluded that although a pooled moderate effect of training on TSH levels was observed when all the studies were analysed using a continuous measure analysis SMD model, an individual analysis of the studies revealed a mild effect, with many studies also revealing the negative impact of training on TSH levels. Nonetheless, a review of the literature revealed that exercise-based intervention strategies are safe and effective as a management strategy for hypothyroidism and obesity due to hypothyroidism.

COMPETING INTEREST:
The authors declared no competing interest.

AUTHORS' CONTRIBUTION:
BH, SF: Conception and design, acquisition, analysis and interpretation of data.
BH, BA: Drafting the article and revising it critically for important intellectual content.
All authors approved the final version of the manuscript to be published.

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