

**A Prospective Observational Study of Sick Euthyroid Syndrome in Acute Myocardial Infarction and Its Prognostic Significance**Aitha Raghaveni<sup>1</sup>, Narahari G<sup>2</sup>, Karankoti Raj Kumar<sup>3</sup><sup>1,2,3</sup>Assistant Professor of Medicine, Government Medical College / Hospital, Sangareddy

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Conflict of interest: Nil

**Abstract:****Aim of the Study:** To find out the occurrence of sick euthyroid syndrome in acute myocardial infarction and prognostic significance of its positive results in myocardial infarction.**Material & Methods:** A total of 65 patients were enrolled for the study from the patients admitted to coronary care unit Tertiary Care Hospital, Telangana State from the period January 2019 to December 2020. 15 patients were excluded as per exclusion criteria. The remaining 50 patients, who satisfied all the inclusion criteria were selected for the study and followed for one week.**Results:** In our study 42% of ST elevation MI patients had sick euthyroid syndrome. So occurrence of sick euthyroid syndrome in our patients 42%. pvalue was 0.258. Sick euthyroid syndrome was 60% among females and 37.5% among males. This observation was statistically insignificant with the p value of 0.50**Conclusion:** The sick euthyroid syndrome positivity rate is proportional to the severity of cardiac damage (as evidenced by KILLIP class and Ejection fraction) and may have a possible prognostic value. Thus sick euthyroid syndrome positivity may contribute to the elaboration of an AMI severity index.**Keywords:** Sick Euthyroid Syndrome (SES); Acute Myocardial Infarction (AMI); Thyroid Stimulating Hormone (TSH).

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**Introduction**

Sick euthyroid syndrome can be described as abnormal findings on thyroid function tests that occur in the setting of a nonthyroidal illness (NTI) without pre-existing hypothalamic-pituitary and/or thyroid gland dysfunction [1].

A decreased level of serum total triiodothyronine (T3) is the most common thyroid function abnormality in patients with acute illness and can be detected within 2 hours after the onset of severe physical stress. As the severity of illness progresses, there is gradual development of a more complex syndrome associated with low levels of T3 and thyroxine (T4).

Levels of thyrotropin (TSH) remain unchanged or slightly reduced. The conversion of the pro-hormone (Thyroxine, T4) to the active form is reduced due to decreased 5'-deiodinase activity peripherally and production of reverse T3 (rT3), the inactive metabolite, is increased [2]. These thyroid hormone changes may be mediated in part by cytokines or other inflammatory mediators, acting at the level of the hypothalamus and pituitary, the thyroid gland, and the hepatic deiodinase system, as well as on binding of thyroxine to thyroid

binding globulin (TBG) [3]. It remains unresolved whether the hormone responses in the sick euthyroid syndrome represent part of an adaptive response, which lowers tissue energy requirements in the face of systemic illness, or a maladaptive response, which induces damaging tissue hypothyroidism [4].

Consequently, the use of thyroid hormone therapy in the sick euthyroid syndrome is controversial. Recovery from the underlying illness is accompanied by disappearance of the thyroid abnormalities. Altered thyroid hormone levels have been reported in starvation, acute and chronic medical illnesses, bone marrow transplantation, surgery, trauma, myocardial infarction and, in fact, can be seen in any severe systemic illness. The more profound the changes in hormone pattern, the poorer the prognosis [5-6]. Sick euthyroid syndrome has also been demonstrated in acute myocardial infarction and a correlation between the severity of the cardiac damage and the degree of the change in thyroid hormones was postulated.

The aim of the present investigation is to study the occurrence of Sick Euthyroid syndrome in patients

with ST elevation myocardial infarction and to evaluate whether the presence of sick euthyroid syndrome in these patients have any prognostic significance in determining severity of AMI.

#### Aim of the Study

1. To study the occurrence of sick euthyroid syndrome in patients with acute myocardial infarction admitted in acute medical care in Osmania General Hospital, Hyderabad.
2. To evaluate whether the presence of sick euthyroid syndrome in these patients have any prognostic significance in determining severity of Myocardial Infarction.

#### Material & Methods

This study was conducted in the Tertiary Care Hospital, Telangana State in collaboration with Department of Cardiology and Department of biochemistry. It was a prospective study done

during the period from January 2019 – December 2020. 50 patients with history, clinical features suggestive of ST elevation myocardial infarction were selected irrespective of age and sex.

**Inclusion Criteria:** Patients with Acute MI patients admitted in acute medical care both males and females of any age

#### Exclusion Criteria

1. Patients with past or present history of thyroid dysfunction.
2. Patients taking drugs that will affect thyroid function
3. Patients with chronic renal failure
4. Patients with decompensated liver disease
5. Patients with thyroid function test suggestive of primary Hypothyroidism and Hyperthyroidism.

#### Results

**Table 1: Types of MI and Sick Euthyroid Syndrome**

	SES +ve	Percentage	SES –ve	Percentage	Total
AWMI	10	36%	18	64%	28
IWMI	8	42%	11	58%	19
Others	2	100%	-	-	3

**Table 2: KILLIP Class and Mean Level of Hormones**

	Mean T3 level ng/ml		Mean T4 level ng/ml		Mean TSH level	
	ng/ml	Std devi	ng/ml	Std devi	Mic unit/ml	Std devi
KILLIP 1	0.91 (28)	.43302	90 (28)	17.5778	1.71 (28)	1.19447
KILLIP 2	0.63 (17)	.31924	70 (17)	20.8148	1.46 (17)	0.70425
KILLIP 3	0.43 (3)	.08145	60 (3)	12.490	1.43 (3)	0.75719
KILLIP 4	0.39 (2)	.04243	52 (2)	28.282	.60 (2)	0.42426
P Value	0.031**		0.001**		0.474	

**Table 3: ICU Stay and Sick Euthyroid Syndrome**

Sick Euthyroid Syndrome	Mean days	No.	Std. Deviation
NEG	3.4483	29	1.12078
POS	4.3889	18	1.09216
Total	3.8085	47	1.19124

**Table 4: Diabetes and Sick Euthyroid Syndrome**

Diabetes	SES +Ve	Percentage	SES –Ve	Percentage	Total
Present	6	60%	4	40%	10
Absent	15	37.5%	25	62.5%	40
Total	21		29		50

**Table 5: Hypertension and Sick Euthyroid Syndrome**

Hypertension	SES +Ve	Percentage	SES –Ve	Percentage	Total
Present	11	58%	8	42%	19
Absent	10	32%	21	68%	31
Total	21		29		50

**Table 6: Smoking and Sick Euthyroid Syndrome**

Smoking	SES +Ve	Percentage	SES –Ve	Percentage	Total
Present	11	41%	16	59%	27
Absent	10	43%	13	57%	23
Total	21		29		50

**Table 7: Alcohol Intake and Sick Euthyroid Syndrome**

Alcohol	SES +Ve	Percentage	SES -Ve	Percentage	Total
Present	9	39%	14	61%	23
Absent	12	44%	15	56%	27
Total	21		29		50

**Table 8: Total Cholesterol Level and Sick Euthyroid Syndrome**

Diabetes	SES +Ve	Percentage	SES -Ve	Percentage	Total
<200 mg/dl	10	53%	9	47%	19
200 to 239 mg/dl	4	25%	12	75%	16
>240 mg/dl	7	47%	8	53%	15
Total	21		29		50

**Table 9: Triglyceride Level and Sick Euthyroid Syndrome**

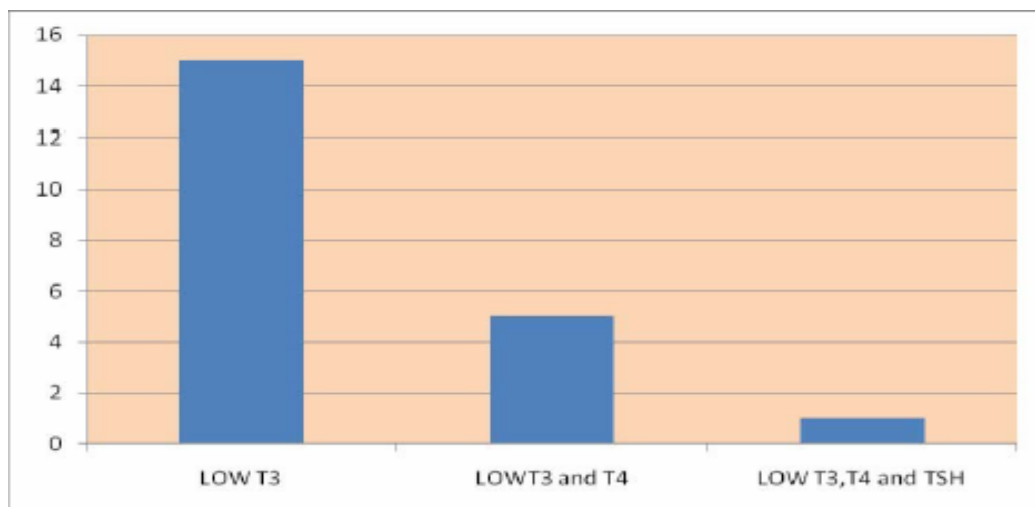
Triglyceride	SES +Ve	Percentage	SES -Ve	Percentage	Total
<200 mg/dl	17	46%	20	54%	37
> 200 mg/dl	4	31%	9	69%	13
Total	21		29		50

**Table 10: HDL Level and Sick Euthyroid Syndrome**

Triglyceride	SES +Ve	Percentage	SES -Ve	Percentage	Total
<40 mg/dl	11	46%	13	54%	24
> 40 mg/dl	10	38%	16	62%	26
Total	21		29		50

**Table 11: Death and Sick Euthyroid Syndrome.**

	SES +ve	Percentage	SES-Ve	Percentage	Total
<b>Male</b>	<b>2</b>	<b>100%</b>	-	-	<b>2</b>
<b>Female</b>	<b>1</b>	<b>100%</b>	-	-	<b>1</b>



**Graph 1: Thyroid Hormone Status in Sick Euthyroid Patients**

**Discussion**

In our study 42% of acute ST elevation MI patients had sick euthyroid syndrome. So occurrence of sick euthyroid syndrome in our patients was 42%. p value was 0.258. So occurrence of sick euthyroid positivity rate was not statistically significant. This implies that occurrence of sick euthyroid positivity rate may vary. In Eber B et al [7] the occurrence of sick euthyroid syndrome in patients with acute myocardial infarction has been reported was 40 %.

In overall the occurrence of one or more abnormalities of thyroid function tests in patients

with non-thyroidal medical illnesses like starvation, sepsis, surgery, myocardial infarction, CABG surgery, bone marrow transplantation, etc. has been reported from 40% to 70%. In our study occurrence of sick euthyroid syndrome was 60% among females and 37.5% among males. This observation was statistically insignificant with the p value of 0.50. In previous studies also the occurrence of sick euthyroid syndrome in sex distribution was same.

In our study in the age group of 20 to 39, no one had sick euthyroid syndrome. In the age group of 40 to 59, 37% had sick euthyroid syndrome. In the

age group of >60, 55% of patients had sick euthyroid syndrome. P value was 0.206 that statistically insignificant. So In our study age group does not influence the occurrence of sick euthyroid syndrome positivity.

In our study occurrence of sick euthyroid syndrome in AAMI patients was 36%, in IAMI patients was 42% and in others 100%. p value was 0.20 that statistically insignificant. So In our study type of MI does not influence the occurrence of sick euthyroid syndrome positivity. To the best of our knowledge no study compared the type of MI and sick euthyroid syndrome. In Killip T, Kimball JT et al [8] study, KILLIP CLASS predicted the severity and mortality in acute coronary syndrome. In Killip class I the mortality rate was 6%, Killip class II was 17%, Killip class III was 38% and Killip class IV was 81%.

In our study patients who presented with KILLIP 1 the sick euthyroid syndrome occurrence was 25%, in KILLIP 2 was 59%, in KILLIP 3 was 67% and KILLIP 4 was 100%. p value was 0.05\* that statistically significant between the KILLIP 1 and KILLIP 2.

In our study KILLIP 2 patients had (higher mortality and morbidity) higher occurrence of sick euthyroid syndrome (59%) to KILLIP 1(25%) This observation was statistically significant with P value of 0.05\*.

In our study 47.6% of sick euthyroid positive patients are in KILLIP 2. But sick euthyroid negative patients only 24.1% are in KILLIP 2. p value was 0.032\*\* that statistically significant. In Killip T, Kimball JT et al study, higher the KILLIP CLASS higher the severity and mortality in acute coronary syndrome reported.

In our study Sick euthyroid syndrome positivity patients have higher KILLIP class than negative patients. Considering this Sick euthyroid syndrome positivity status predicts the severity and mortality in acute MI.

In our study Mean T3 level, Mean T4 level, Mean TSH level progressively decreased in patients who presented with increased severity as evidenced by KILLIP class. The decrease of Mean level of T3, T4 in various class of KILLIP was statistically significant. The decrease of Mean level of TSH in various class of KILLIP was statistically insignificant. In Pavlou HN et al [9]. *Angiology* 2002; 53: 699-707. Study also observed that progressive decrease of Mean T3 level, Mean T4 level and Mean TSH level with increased severity of myocardial infarction in which severity was assessed by KILLIP class. In Friberg L et al [10] *Arch Intern Med* 2002; 162: 1388-1394. Study observed that mortality was high among patients with the most pronounced thyroid level depression.

Medha Rajappa and S.K. Sen et al [11] Study concluded that occurrence of sick euthyroid syndrome and the degree of T3 decrease is proportional to the severity of cardiac damage and may have a possible prognostic value, so analyzing various studies our study also predicts the severity by more suppression of thyroid hormone.

In our study, patients presented with LVEF<50 the occurrence of sick euthyroid syndrome was 60% and patients who presented with LVEF>50 was 24%. In our study, patients who presented with LVEF<50 the sick euthyroid syndrome positivity was high compare to high LVEF >50. p value was 0.01\*\* that statistically significant.

In our study 71.4% of sick euthyroid positive patients are in LVEF<50 But 34.5% of sick euthyroid negative patients only in this group. p value was 0.010\*\* that statistically significant. In Hallstrom A et al [12]. *J Am Coll Cardiol.* 1995 May; 25: 1250-7. study concluded that low left ventricular ejection fraction are strongly associated with morbidity and mortality after acute myocardial infarction. Sick euthyroid positive patients are high likelihood to have LVEF<50. So the sick euthyroid syndrome positivity predicts the high mortality and morbidity than negative individuals in acute myocardial infarction.

In our study, patients who presented with LVEF<50 Mean T3 level, Mean T4 level, Mean TSH level were moderately low compared to patients who presented with LVEF>50. In our study patients who presented with the LVEF <50 and LVEF>50 the decrease of Mean T3 level, Mean T4 level and Mean TSH level between these groups was statistically significant.

In Medha Rajappa and S.K. Sen et al *Biomedical Research* 2005; 16 (1): 15- 18 study observed that extent of decrease of Mean T3 level ,Mean T4 level, Mean TSH level was more significant in patients in group I (with LVEF < 50%), who have a worse prognosis than those in group II.

So analyzing various studies our study also observed when the severity was increased as evidenced by low LVEF more suppression of thyroid hormone level occurs.

In our study in sick euthyroid positive patients mean ICU stay duration was 4.39 days compare to sick euthyroid syndrome negative patients in whom mean ICU stay duration was 3.45 days with p value of 0.007\*\* so this observation was statistically significant. This implies that sick euthyroid positive patients have high morbidity. In our study patients who had DIABETES the occurrence of sick euthyroid syndrome was 60% and patients who presented with NO DIABETES the occurrence of sick euthyroid syndrome was 37.5%. The p value was insignificant. So in our study the

presence of DIABETES does not influence the occurrence of sick euthyroid syndrome.

In our study patients who had HYPERTENSION the occurrence of sick euthyroid syndrome was 58% and patients who presented with NO HYPERTENSION the occurrence of sick euthyroid syndrome was 32%. The p value was insignificant. So in our study the presence of HYPERTENSION does not influence the occurrence of sick euthyroid syndrome.

In our study patients with risk factor SMOKING the occurrence of sick euthyroid syndrome was 41%, patients who presented with NO SMOKING the occurrence of sick euthyroid syndrome was 43%. The p value was insignificant. So in our study the presence of SMOKING habit does not influence the occurrence of sick euthyroid syndrome. In our study patients who had ALCOHOL intake the occurrence of sick euthyroid syndrome was 39%, patients who presented with no H/O of ALCOHOL intake the occurrence of sick euthyroid syndrome was 44%. The p value was insignificant. So in our study the H/O ALCOHOL intake does not influence the occurrence of sick euthyroid syndrome.

In our study patients who presented with fasting cholesterol level <200 mg/dl the occurrence of sick euthyroid syndrome was 53%, fasting cholesterol level 200 to 239mg/dl the occurrence of sick euthyroid syndrome was 25% and fasting cholesterol level >240mg/dl the occurrence of sick euthyroid syndrome was 47%. p value was 0.50 that statistically insignificant. So in our study cholesterol level does not influence the sick euthyroid positivity.

In our study patients who presented with fasting TRIGLYCERIDE level <200 mg/dl the occurrence of sick euthyroid syndrome was 46% and fasting TRIGLYCERIDE level >200mg/dl the occurrence of sick euthyroid syndrome was 31%. p value was 0.50 that statistically insignificant. So in our study TRIGLYCERIDE level does not influence the sick euthyroid positivity. In our study patients who presented with fasting HDL level <40mg/dl the occurrence of sick euthyroid syndrome was 46% and fasting HDL level >40mg/dl the occurrence of sick euthyroid syndrome was 38%. p value was 0.50 that statistically insignificant. So in our study HDL level does not influence the sick euthyroid positivity.

In our study occurrence of sick euthyroid syndrome among death patients was 100%.

- Mean T3 level in death patients was 0.39ng/ml.
- Mean T4 level in death patients was 58ng/ml.
- Mean TSH level in death patients was 0.7micro unit/ml.

In our study, sick euthyroid syndrome positive patients had Mean T3 level - 0.41ng/ml, Mean T4 level - 69ng/ml, Mean TSH level -1.33micro unit /ml, sick euthyroid syndrome negative patients, had Mean T3 level -1.02ng/ml, Mean T4 level - 87ng/ml, Mean TSH level -1.73micro unit /ml. On comparison between the groups of sick euthyroid positive and negative patients, the decrease of Mean T3, Mean T4 level in sick euthyroid positive patients was statistically significant as evidenced by p value. But the decrease of Mean TSH level in sick euthyroid positive patients was statistically insignificant.

In our study, in sick euthyroid syndrome positive patients repeat thyroid function test done at Day 7, the Mean T3 level was 0.68ng/ml, Mean T4 level was 84ng/ml and Mean TSH level was 1.61micro unit /ml.

This observation was statistically significant when we compare to Mean T3, Mean T4 and Mean TSH was done at Day 1. This observation confirms the occurrence of sick euthyroid syndrome and indicates it was transient manifestation.

### Conclusion

- Occurrence of sick euthyroid syndrome was common in acute ST elevation myocardial infarction patients.
- Our study shows that of 42% acute ST elevation myocardial infarction patients had sick euthyroid syndrome positivity.
- The commonest abnormalities is found to be a low level of total T3 as demonstrated in our study where 71% of the patients had low level total T3.
- The next most common abnormalities is found to be both low level of total T3 & total T4(24%).
- As the severity of the illness increases sick euthyroid syndrome positivity rate was increased. (KILLIP 1 sick euthyroid syndrome positivity was 25%, in KILLIP 2 patients positivity was 59%, in KILLIP 3 patients was 67% and KILLIP 4 patient was 100%. patients presented with LVEF<50 the positivity of sick euthyroid syndrome was 60% and patients presented with LVEF>50 was 24%).
- The degree of T3 decrease is proportional to the severity of cardiac damage and may have a possible prognostic value. (LVEF<50 Mean T3 level 0.62 ng/ml, LVEF>50 Mean T3 level 0.9ng/ml).
- The changes in the thyroid hormone status return to normal once the patient recovers from the critical illness.
- Though these patients have abnormalities in the thyroid hormone status they are clinically euthyroid.

- Thyroid hormone system is rapidly down regulated in acute myocardial infarction. This may be beneficial during acute ischemia.
- The sick euthyroid syndrome positivity rate is proportional to the severity of cardiac damage (as evidenced by KILLIP class and Ejection fraction) and may have a possible prognostic value. Thus sick euthyroid syndrome positivity may contribute to the elaboration of an AMI severity index.
- The role of thyroid hormone replacement as a method of treatment of sick euthyroid syndrome is still controversial and there are no proper studies to recommend this.
- Treatment of underlying condition is the treatment of choice.

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