HYPOTHYROIDISM AND AGEING EFFECT ON PULMONARY ARTERY SYSTOLIC PRESSURE
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ABSTRACT

BACKGROUND
Hypothyroidism is a cause of pulmonary artery hypertension. Increased BMI also contributes to pulmonary artery hypertension. Increasing age in healthy people is associated with increasing pulmonary artery pressures.

MATERIALS AND METHODS
We studied 30 subjects of hypothyroidism and 50 healthy controls; mean age was 39.53 ± 14.97 and 38.82 ± 14.65 years respectively. 27 females and 3 males were hypothyroid. 44 females and 6 males were controls.

RESULTS
Pulmonary artery systolic pressure (PASP) was significantly more in hypothyroid individuals as compared to controls, p-value 0.01, mean PASP in hypothyroid individual was 25.83 ± 6.30 mmHg and in controls it was 23.12 ± 2.97 mmHg. Effect size by r square 0.08.

Higher BMI was associated increased PASP in hypothyroid individual. P value 0.01. Effect size by r square 0.11, mean BMI was 24.54 ± 3.95 kg and mean PASP was 25.83 ± 6.30 mmHg.

Increasing age was associated with increased PASP in controls. P value 0.01, effect size by r square 0.38; mean age was 38.82 ± 14.65 years and mean PASP was 23.12 ± 2.97 mmHg.

CONCLUSION
Hypothyroidism is associated with increase in pulmonary artery systolic pressure. Increased BMI of hypothyroid has more effect on increased pulmonary artery systolic pressure than hypothyroidism alone. In healthy subjects, pulmonary artery systolic pressure increases with age.

KEYWORDS
BMI, Hypothyroidism, Pulmonary Hypertension.

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BACKGROUND
Association of thyroid disease with pulmonary artery hypertension is known; thyroid disease is considered as aetiology of pulmonary hypertension by clinical classification of pulmonary hypertension established at the consensus meeting held in 2003 in Venice, Italy. But there are no studies which have looked for occurrence of pulmonary artery hypertension in patients of hypothyroidism, of course there are studies of cases of pulmonary hypertension, where the increased occurrence of hypothyroidism is present. So in this current study, we evaluated occurrence of pulmonary artery hypertension in patients of hypothyroidism. Association of pulmonary artery hypertension and autoimmune disease is postulated, and thus hypothyroidism which is autoimmune disease and pulmonary artery hypertension can be correlated. Association of Raynaud's phenomenon and idiopathic pulmonary artery hypertension is known, and there is link between thyroid disease and Raynaud's phenomenon. Increased BMI, hypoventilation and hypoxia are associated with hypothyroidism and this can influence pulmonary artery pressure.

Aims and Objectives
1. To evaluate increased pulmonary artery systolic pressure in patients of hypothyroidism.
2. To correlate increased BMI of hypothyroid patients with pulmonary artery systolic pressure.
3. To correlate increased pulmonary artery systolic pressure with increasing age in healthy controls.

MATERIALS AND METHODS
Study Design- This was a hospital based prospective study.

Study Participants and Sample Size- 30 patients of hypothyroid and 50 healthy controls were included, during the study period from January 2013 to December 2013. For

the purpose of convince subjects with hypothyroidism and healthy controls were labelled as conditions.

**Study Variables**- Pulmonary artery systolic pressure was estimated by echocardiography. Peak Tricuspid jet velocity was used for calculation. RA pressure of 5 mmHg was added to TR jet velocity to derive pulmonary artery systolic pressure. All patients of hypothyroid underwent blood test for T3, T4, TSH and BMI estimation.

**Statistical Analysis**- SPSS version 17 and G power software were used to evaluate the study. P value was set to less than 0.05 to prevent alpha error. Power required was set to be more than 80% to prevent beta error. Means were expressed as mean ± standard deviation. Effect size was expressed by r square value 0.01 to 0.08 small, 0.09 to 0.24 considered medium more than 0.25 large effect.

**Inclusion and Exclusion Criteria**
Subjects included were newly diagnosed cases of hypothyroid during the study period and also the cases of hypothyroid diagnosed or on treatment within six months duration.

Cases of hypothyroid diagnosed and on treatment for more than 6 months were excluded from study. Patients of Chronic obstructive pulmonary disease, known cases of connective tissue diseases and underlying cardiac diseases like cardiomyopathy, valvular heart disease were excluded from the study.

50 cases of healthy controls were also included.

**Baseline Characteristics of Subjects**
In hypothyroid group of 30 subjects, 27 were females and 3 were males, and among control group, 44 were females and 6 were males. See Table 1.

<table>
<thead>
<tr>
<th>Condition</th>
<th>Mean of Age</th>
<th>N</th>
<th>Std. Deviation</th>
<th>Minimum</th>
<th>Maximum</th>
<th>Range</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypothyroid</td>
<td>39.53</td>
<td>30</td>
<td>14.97</td>
<td>18</td>
<td>67</td>
<td>49</td>
<td>0.83</td>
</tr>
<tr>
<td>Control</td>
<td>38.82</td>
<td>50</td>
<td>14.65</td>
<td>18</td>
<td>67</td>
<td>49</td>
<td></td>
</tr>
</tbody>
</table>

**RESULTS**
PASP between Hypothyroids and controls.

Pulmonary artery systolic pressure (PASP) was significantly more in patients of hypothyroid as compared to controls, P value was 0.033, mean PASP in hypothyroid individuals was 25.83 ± 6.30 mmHg and in controls it was 23.12 ± 2.97 mmHg.

Effect size by r square was 0.08 so it had small effect see table 3.

**BMI and PASP in Hypothyroids**
Correlation of BMI with PASP in hypothyroid patients by non-parametric bivariate analysis was significant. P value was 0.01. Effect size by r square was 0.11 so it had medium effect. Mean BMI was 24.54 ± 3.95 kg and mean PASP was 25.83 ± 6.30 mmhg see table 4 and figure 1.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Condition</th>
<th>N</th>
<th>Mean</th>
<th>Std. Deviation</th>
<th>Karl Pearson’s Correlation Coefficient r- Value</th>
<th>p- Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI</td>
<td>30</td>
<td>24.54</td>
<td>3.959</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2D Echo PASP value (mm Hg)</td>
<td>30</td>
<td>25.83</td>
<td>6.303</td>
<td>0.638</td>
<td>P&lt;0.01, Significant</td>
<td></td>
</tr>
</tbody>
</table>
PASP and Age in Controls
We also did Karl Pearson Correlation for age and PASP in healthy controls. It showed significant correlation with PASP with age. P value was 0.01 see Table 5 and Figure 2, effect size by r square value was 0.38 it was large effect. Mean age was 38.82 ± 14.65 years and mean PASP was 23.12 ± 2.97 mmHg.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>N</th>
<th>Mean</th>
<th>Std. Deviation</th>
<th>Karl Pearson's correlation coefficient r - value</th>
<th>p-value</th>
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</thead>
<tbody>
<tr>
<td>Age</td>
<td>50</td>
<td>38.82</td>
<td>14.648</td>
<td></td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>2D Echo PASP value (mm Hg)</td>
<td>50</td>
<td>23.12</td>
<td>2.974</td>
<td>0.614</td>
<td>significant</td>
</tr>
</tbody>
</table>

Table 5. Table Showing Karl Pearson Correlation for Age and PASP in Controls

DISCUSSION
To our best knowledge, this study was first of its kind to evaluate pulmonary artery systolic pressure in hypothyroid patients. Pulmonary artery systolic pressure was significantly more in hypothyroid subjects as compared to healthy controlled subjects. But the effect size (r square) was small i.e. 0.08. this is in accordance from predication from study by Curnock A et al., but Curnock AL studied, patients of pulmonary artery hypertension and looked for occurrence of hypothyroidism. It was retrospective study of 41 patients of pulmonary hypertension, of them 22.5% had evidence of hypothyroidism, which was significantly more compared general population. So they suggested to check thyroid profile in patients of pulmonary hypertension.

High BMI is suggested as cause of pulmonary hypertension. In patients of hypothyroidism increased BMI is established fact. We evaluated effect size of BMI in hypothyroid subjects, it was medium i.e. 0.11, as compared
to small effect size 0.08 of hypothyroidism. So we hypothesized in hypothyroid patient it is increased BMI, responsible for increase in pulmonary artery systolic pressure, rather than direct hypothyroidism itself. Of course this hypothesis needs further study.

Otherwise normal subjects, systemic systolic pressure is known to increase with age. Likewise pulmonary artery systolic pressure also increases with age. To check this hypothesis we evaluated our healthy control group for age wise increase in pulmonary artery systolic pressure. It was found to positively associated with large effect size 0.38. This was in accordance with study by Carolyn S.P et al. That was prospective study of healthy subjects followed up for 9 years. Among 1413 subjects (69%) with measurable PASP (age, 63±11 years; 43% male), median PASP was 26 mm Hg (25th to 75th percentile, 24 to 30 mm Hg) and increased with age (r=0.31, P<0.001). Those with increased PASP had higher mortality. In another study of 322 subjects mean pulmonary artery pressures increased progressively with age: 16.7 ± 4.6, 17.9 ± 6.4 and 20.6 ± 8.0 mm Hg for those aged less than 45 years (n = 50), 45 to 64 years(n = 238) and more than 65 years (n = 34), respectively (p = 0.020).

CONCLUSION
Hypothyroidism is associated with increase in pulmonary artery systolic pressure. Increased BMI of hypothyroid has greater effect on increased pulmonary artery systolic pressure than hypothyroidism alone. In healthy subjects, pulmonary artery systolic pressure increases with age.

Limitation
We did not evaluate effect of BMI on pulmonary artery systolic pressure in healthy controls. At baseline post hoc power of t test done for control versus hypothyroids with regard to age did not reach sufficient power; so we need further study with larger sample.

REFERENCES