Six categories of the baseline questionnaire administered by AlphNet:

1. Demographic information and specified genotype and assemblment status (index vs. non-index)
2. Work and productivity (employment, disability and productivity scale)
3. Pulmonary symptoms, current treatment, exacerbation frequency and medications
4. Details of augmentation therapy and lung and liver transplant data (if any). Complete data on augmentation therapy was not available for this study.
5. Self-perceived fitness and health and smoking and drinking habits
6. Comorbidities as its causes, and compliance with AlphaNet’s Disease management program (ADMAPP) and Big Fat Reference Guide (BFRG).

<table>
<thead>
<tr>
<th>Variable</th>
<th>ZZ (n=2554)</th>
<th>SZ (n=323)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>56.5 ± 11.4</td>
<td>56.3 ± 11.3</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Male</td>
<td>1493 (58.3)</td>
<td>130 (40.3)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>2460 (96.2)</td>
<td>277 (85.8)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Black</td>
<td>94 (3.8)</td>
<td>46 (14.2)</td>
<td></td>
</tr>
<tr>
<td>Smoking status</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current smoker</td>
<td>2207 (86.5)</td>
<td>168 (51.9)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Former smoker</td>
<td>362 (14.2)</td>
<td>134 (41.3)</td>
<td></td>
</tr>
<tr>
<td>Never smoker</td>
<td>85 (3.3)</td>
<td>21 (6.5)</td>
<td></td>
</tr>
<tr>
<td>Compliant with % of ADMAPP</td>
<td>39.6 ± 10.4</td>
<td>38.2 ± 10.6</td>
<td>&lt;0.001*</td>
</tr>
</tbody>
</table>

Summary of sample baseline characteristics according to genotype.

Differences Between ZZ and SZ patients on the AlphaNet Program

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INTRODUCTION

α1-Antitrypsin deficiency (AATD):
- autosomal co-dominant disorder
- results from mutations of the SERPINA1 gene
- typically associated with the increased risk of early onset pulmonary emphysema in adult population, liver disease in children as well as adults and, more rarely, pancreatitis

the most common mutations associated with AATD are PiZ and PiS mutations

AATD was first discovered in 1963 by Laurent and Eriksson. It is considered a common genetic disorder; however, it is still often undiagnosed.

MATERIALS AND METHODS

Our study population consisted of members of AlphaNet - a for-profit health management company that coordinates management and treatment of Alpha-1 antitrypsin deficient patients.

The results for categorical variables were reported by frequencies and proportions, and for continuous variables as mean ± SD (min. max). Values between the groups were compared using t-test and ANOVA, and C2 compared test respectively. SAS software (SAS 9.4 for Windows) was used for the statistical analysis.

The significance level was set at 0.05.

RESULTS

- ZZs were slightly younger than their SZ counterparts.
- As anticipated, serum levels of Alpha-1 Antitrypsin in ZZs were higher
- ZZs report heavier and longer history of smoking compared to Pizzs

Our study found significant differences in comorbidities between the two genotypes with greater proportion of patients with SZ phenotype in our cohort were diagnosed with high blood pressure, diabetes, congestive heart failure and cerebrovascular disease compared to the patients with ZZ phenotype.

- self-perceived health and fitness. Adherence to ADMAPP program
- greater proportion of patients with PiSZ compared to Pizzs view themselves being overweight and out of shape
- higher proportion of patients with PiSZ consider themselves being in “poor health” compared to Pizzs
- greater proportion of the patients with PiSZ compared to Pizzs report following ADMAPP program

Index ZZs were more frequently unable to work due to their medical condition and reported to miss greater number of days from work due to illness. Higher proportion of index ZZ cases received disability benefits (60.2% vs. 56.8%, p=0.007).

Higher number of index Pizz patients reported ever smoked compared to non-index cases (74.1% vs. 66% (p=0.001), with greater number of years smoked.

DISCUSSION

- The present research is one of a few studies in North America that focuses on looking into the differences and similarities not only between genotypes but also between index and non-index cases.
- Our study detected differences in disease progression and quality of life measures, as well as genotypes stratified by indices ZZ and SZ conditions
- Augmentation therapy with human serum derived α1-antitrypsin still remains the only specific treatment option for patients with AATD, aiming at the prevention of pulmonary disease progression and increasing survival.
- As anticipated, greater proportion of the patients with ZZ were receiving treatment than SZ which might be explained by significantly lower mean plasma ADMAPP AAT levels among ZZs.
- Our study demonstrated that patients with ZZ and SZ genotypes significantly differ in their perception of health and fitness as well as their health behaviors
- Compared to ZZs, SZ patients present with significantly higher prevalence of cardiovascular comorbidities, including hypertension, cerebrovascular disease, as well as congestive heart failure, diabetes, arthritis. This association with phenotype is not well understood, nor sufficiently investigated previously.
- Greater proportion of SZs (compared to ZZs) view themselves as “overweight”, “out of shape” and “in poor health”, however they exercise less and report heavier and longer history of smoking compared to ZZs.
- Significantly lower proportion of SZ patients compared to ZZs report following the guidelines of ADMAPP - a vital component aimed to improve patients’ health outcomes. This lower adherence to the program may be due to the concept of the low self-perceived seriousness of their condition compared to the more severe ZZ mutation.

CONCLUSION

In summary, the main take away message of this study was that ZZ and SZ patients differ not only in serum levels of their Alpha-1 antitrypsin levels, but in their self-perception of quality of life as well as their health behaviors, adherence to management program and other characteristics.

Despite the availability of the ADMAPP program and other resources directed on improvement of the quality of life of the patients with AATD, it appears that more severely affected ZZ individuals adhere to ADMAPP recommendation and maintain healthier lifestyles that are known to improve the overall quality of life of the patients with this disorder.