**Machine Learning Quest for Predictive Markers of Lifestyle Modification Outcomes in Pediatric Obesity Treatment**

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**INTRODUCTION**

The traditional approach to childhood obesity management is lifestyle modification/LSM. Nevertheless, the response rate is variable and difficult to predict.

**AIM**

A systematic search for markers to predict outcomes of simple LSM in pediatric obesity management.

**PATIENTS & METHOD**

Out of 240 children with obesity (BMI>97%), recruited to a prospective multi-OMICS study granted by ESPE Research Unit, 159 subjects (age 8-17 yrs, median 12.8 yrs; 45% females) finished twelve-months of LSM obesity management at three clinical centers in three countries. Their baseline (VO) phenotype was precisely described with more than 180 clinical and laboratory features grouped as markers of:
- general description,
- family and patient’s history,
- lifestyle/LS,
- socioeconomic status/SES,
- body composition/BC,
- insulin resistance/IR,
- liver diseases/LD,
- metabolic syndrome/MetS,
- steroid metabolome
- gut microbiome.

Additional 150 features were measured at V3/V6/V12 months.

Machine learning technique/CART as implemented in ‘rpart’ & ‘rpart.plot’ R packages was applied to build & visualize decision trees to automatically identify the markers and their cut-offs with the strongest correlation to a “success” of LSM, defined as a decrease in z-score BMI V12-V0.

Odds Ratio (OR) and P-values (p) were calculated by Fisher’s Exact test

**RESULTS**

118 out of 159 (74.2%) participants were classified as responders as responders to LSM.

- When built on the IR & LD features, a decision tree pointed to a strongest role of the following parameters:
  - acardiacosa nigricans/AN,
  - resistance levels,
  - glucose 120,
  - NAFLD in USG
  - and insulin/glucose ratio.

- The AN feature was significantly associated with the response to LSM (OR 2.75; p=0.0106), where the lack/presence of AN predicted success in 84%/65% cases, resp.

- When the lack of AN was observed simultaneously with resistin value <16 mg/ml the response rate grew to 91% (OR 9.05; p=0.0026), while the presence of AN together with glucose 120<136 mg/dl predicted 93% of the successful outcomes (OR 8.51; p=0.0281).

- On the other extreme, high insulin/glucose ratio ≥0.34 (with the presence of AN together with NAFLD/USG, and with glucose 120<136 mg/dl), decreased the response rate to 23% (OR 0.20; p=0.0452).

- Out of SES & LS features at VO, a small (-6.6hrs) number of sleep hours on schooldays /high frequency of sweet beverages = lack of Physical Activity were found to be associated with the lowest chance for success (success rate 33%/40%, OR 0.15/0.34, p=0.0032/0.013, respectively).

- Leptin > 18 ng/ml and WHHR < 0.66 (MetS & BC features) were putative positive predictive markers.

**CONCLUSIONS**

Insulin resistance features, and history of inappropriate sleep or beverages consumption before intervention are significantly associated with failure of LSM in childhood obesity. Pending the validation on an independent cohort, our findings suggest the predictive role of these markers.

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**CONTACT INFORMATION**

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**Table 1:**

<table>
<thead>
<tr>
<th>Feature</th>
<th>Odds Ratio (OR)</th>
<th>P-value (p)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acardiacosa nigricans/AN</td>
<td>2.75</td>
<td>0.0106</td>
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<tr>
<td>Resistance levels</td>
<td></td>
<td></td>
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<tr>
<td>Glucose 120</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NAFLD in USG</td>
<td></td>
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<tr>
<td>Insulin/glucose ratio</td>
<td></td>
<td></td>
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<tr>
<td>WHHR (≤0.66)</td>
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<tr>
<td>Leptin (&gt;18 ng/ml)</td>
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</tbody>
</table>

**Figures:**

- Decision tree of predictive markers
- Graph of insulin resistance and history of inappropriate sleep or beverages consumption before intervention

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**Image:**

- Map of Europe

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**Figure legends:**

- Decision tree of predictive markers
- Graph of insulin resistance and history of inappropriate sleep or beverages consumption before intervention