# Associations between serum level of total leptin, functional leptin (bio-LEP), soluble leptin receptor and anthropometric parameters in children with severe early-onset obesity (SEOO) – the German-Polish Study (EOL-GPS)

**Agnieszka Zachurzok[1], Ewa Malecka-Tendera[1], Elzbieta Petriczko[2], Artur Mazur[3], Lutz Pridzun[4], Bertram Flehmig[4], Julia von Schnurbein[5], Michael B. Ranke[6], Martin Wabitsch[5], Stephanie Brandt[5]**

**1.** DEPARTMENT OF PEDIATRICS AND PEDIATRIC ENDOCRINOLOGY, MEDICAL UNIVERSITY OF SILESIA, SCHOOL OF MEDICINE IN KATOWICE, KATOWICE, POLAND, **2.** POMERANIAN MEDICAL UNIVERSITY, DEPARTMENT OF PEDIATRICS, ENDOCRINOLOGY AND DIABETES, SZCZECIN, POLAND. **3.** UNIVERSITY OF RZESZOW, DEPARTMENT OF PEDIATRICS, RZESZOW, POLAND. **4.** MEDIAGOST GMBH, REUTLINGEN, GERMANY. **5.** CENTER FOR RARE ENDOCRINE DISEASES, DIVISION OF PEDIATRIC ENDOCRINOLOGY AND DIABETES, DEPARTMENT OF PEDIATRICS AND ADOLESCENT MEDICINE, ULM UNIVERSITY MEDICAL CENTER, ULM, GERMANY. **6**. UNIVERSITY CHILDREN´S HOSPITAL, TÜBINGEN, GERMANY

## BACKGROUND

Severe early-onset obesity (SEOO) is more likely to be caused by genetic factors. Thus those of the leptin pathway should be consider in the diagnostic approach. Leptin is a hormone produced in adipose tissue, involved in energy homeostasis regulation. Disturbances in leptin pathway result in impaired satiety, food-seeking behaviour and hyperphagia, as well as in immune system disorders and hypogonadotropic hypogonadism. Mutations in the leptin gene leading to leptin deficiency as well leptin receptor mutations leading to a functional leptin deficiency were described. Recently in children with SEOO and high total serum leptin level, mutations in the leptin gene were observed, resulting in the production of biologically inactive leptin. Like patients with leptin deficiency these individuals can benefit from recombinant human leptin (metreleptin) treatment.

**The aim of the study was to investigate anthropometrics and leptin parameters, specifically searching for bio-inactive leptin, in children with SEOO.**

## PATIENTS & METHODS

**Study cohort: 50** children (n=22 boys, n=28 girls) who developed a BMI>25kg/m² before an age of 6 years, presented at individual study centers [Germany: n=1, Poland: n=3 (**German-Polish consortium, EOL-GPS**)] between July 2015 and Dec 2017.

**Anthropometric parameters** (weight[kg], height[cm], BMI[kg/m²]) were measured and a serum blood sample was taken. If possible, parental anthropometric parameters (weight[kg], height[cm], BMI[kg/m²]) and blood samples were ascertained.

Levels of total leptin [**totLEP,ng/ml**[1]], functional leptin [**bioLEP**[1,2]] and soluble leptin receptor [**sLEPR**[1]] were measured in serum samples. Quotient of bioLEP/totLEP and LEP-SDS[3] were calculated.

The study was approved by the Local Ethics Committees and informed consent was obtained from every patients' parent.

## RESULTS

**Table 1.** Clinical characteristics (age, BMI, BMI-SDS and leptin parameters) of the children (n=50) and their parents (n=45 mothers, n=43 fathers, n=42 trios)

| | Children | Mothers | Fathers |
|---|---|---|---|
| **Age at blood sampling [years]** | 7.7±4.5 | 37.3±7.0 | 39.3±7.3 |
| **BMI [kg/m²]** | 32.2±9.3 | 31.3±7.8 | 31.2±8.9 |
| **BMI-SDS / BMI>25 kg/m² [%]** | 3.7±0.9 | 76.2% | 83.3% |
| **totLEP [ng/ml]** | 44.0±32.0 | 27.2±20.8 | 14.4±13.8 |
| **bioLEP [ng/ml]** | 41.3±28.3 | 27.6±20.2 | 13.8±13.2 |
| **LEP SDS** | -1.6±2.6 | -0.1±1.5 | -0.3±1.9 |
| **sLEPR [ng/ml]** | 19.9±7.5 | 18.3±7.3 | 20.6±6.0 |
| **bioLEP/totLEP** | 1.0±0.1 | 1.0±0.1 | 1.0±0.1 |

**Table 2.** Correlations between anthropometrics and leptin parameters in children

| Children (n=50) | totLEP | | bioLEP | | bioLEP/totLEP | | sLEPR | | LEP SDS | |
|---|---|---|---|---|---|---|---|---|---|---|
| | r | p | r | p | r | p | r | p | r | p |
| **Gender** | 0.17 | >0.05 | 0.20 | >0.05 | 0.07 | >0.05 | -0.04 | >0.05 | -0.19 | >0.05 |
| **Age at blood sampling** | **0.52** | **<0.05** | **0.50** | **<0.05** | -0.27 | >0.05 | **-0.53** | **<.0001** | -0.18 | >0.05 |
| **BMI** | **0.68** | **<.0001** | **0.67** | **<.0001** | -0.15 | >0.05 | **-0.44** | **<0.05** | **-0.70** | **<.0001** |
| **BMI SDS** | 0.04 | >0.05 | 0.06 | >0.05 | 0.12 | >0.05 | 0.23 | >0.05 | **-0.32** | **<0.05** |
| **totLEP** | - | - | **1.00** | **<.0001** | -0.16 | >0.05 | **-0.39** | **<0.05** | **-0.29** | **<0.05** |
| **bioLEP** | **1.00** | **<.0001** | - | - | -0.10 | >0.05 | **-0.37** | **<0.05** | **-0.28** | **<0.05** |
| **bioLEP/totLEP** | -0.16 | >0.05 | -0.10 | >0.05 | - | - | 0.26 | >0.05 | 0.00 | >0.05 |
| **sLEPR** | **-0.39** | **<0.05** | **-0.37** | **<0.05** | 0.26 | >0.05 | - | - | 0.19 | >0.05 |
| **LEP SDS** | **-0.29** | **<0.05** | **-0.28** | **<0.05** | 0.00 | >0.05 | 0.19 | >0.05 | - | - |

**KEY RESULTS**

1) **We identified no child with leptin deficiency or biologically inactive leptin**
2) **>75% of the parents were overweight/obese**
3) **TotLep concentrations were positively correlated with BMI values (r=0.68, p<0.0001)**
4) **LEP-SDS values were negatively correlated with BMI values (r=-0.70, p<0.0001)**

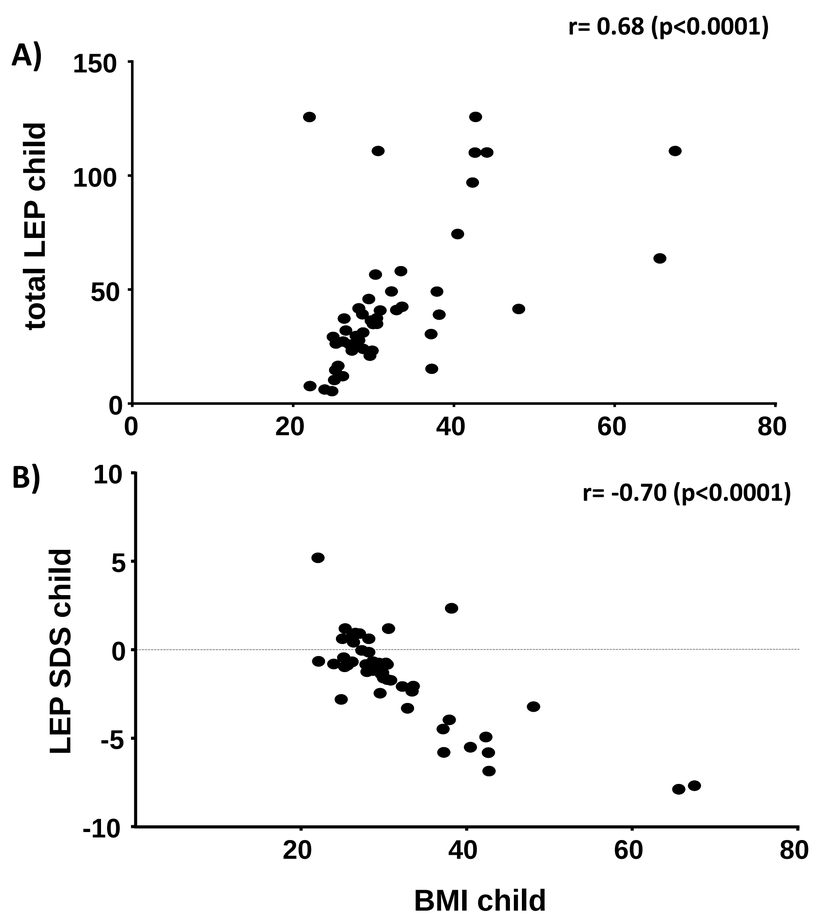


**Figure 1**. Correlations between A) BMI values and total leptin levels and between B) BMI and LEP SDS values in children

## CONCLUSIONS

**Disorders of leptin as a cause of obesity are rare. Also in this cohort with SEOO we identified no new cases of children with leptin deficiency or bio-inactive leptin. We confirmed previously published observations of a negative correlation between sLEPR, age and BMI values in children. The strong negative correlations between LEP-SDS and BMI values could be interpreted as relative leptin resistance at extremes of fat mass. However further collection and analysis of SEOO children must prove whether the relationship between BMI and leptin parameters in these patients is definitely different from normally weighing children.**

[1]Elisa,Mediagnost,Reutlingen,Germany: www.mediagnost.de; [2]Wabitsch et al. Eur J Endocrinol. 2017; 176(3): 315-322; [3]Blum et al. JCEM. 1997; 82(9): 2904-10

## CONTACT

**dr hab n med Agnieszka Zachurzok**
Department of Pediatrics and Pediatric Endocrinology, Medyków St. 16; 40-752 Katowice, POLAND
agnieszkazachurzok@poczta.onet.pl

**AUTHORS HAVE NOTHING TO DISCLOSE**


57ESPE 141--P2
Fat, metabolism and obesity
Agnieszka Zachurzok
Poster presented at: 57th ESPE 2018 Meeting ATHENS GREECE 27-29 September 2018