

Age of obesity onset could be the first indicator of future metabolic complications – preliminary data of prospective multicenter study



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Context The unified approach for obese children can result in therapeutic failure as obesity is a symptom of several conditions. The time of obesity beginning seems crucial. It was previously suggested that only children with obesity onset beyond age ~3 years (around the time of adiposity rebound ~5-7 yrs and *adrenarche* ~6-7 yrs) will develop the metabolic syndrome and T2D. In turn, early childhood obesity (< age 3, but usually within the 1st year of life) carries a lower risk of metabolic syndrome and T2D comparing to that with the onset during juvenility.

Aim We determine the clinical and biochemical profile of early- (E-Ob, up to 3 yrs) and late-onset (L-Ob; after 3 yrs) obesity.

Patients & Methods We analysed detailed clinical and laboratory profiles of a consecutive series of **241** non-syndromic obese children (117 F/124 M; BMI >97%) aged **6.0-17.0**, recruited in 2018 in Italy, Turkey and Poland for the prospective '**multi-OMICS**' study.

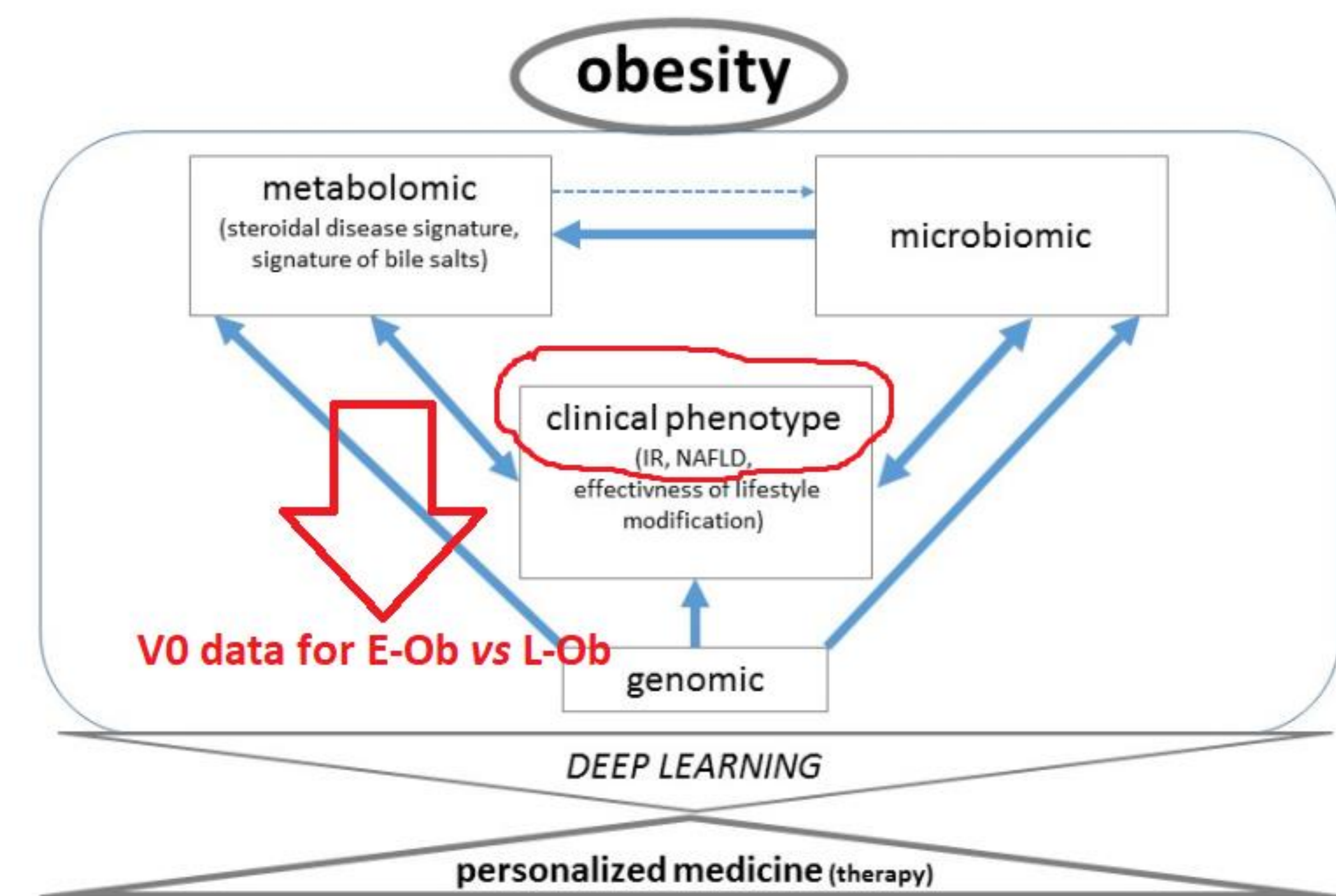


Figure delineating the idea of the **multi-OMICS** project: to develop a personalized approach to childhood obesity by utilizing a high throughput data analysis of steroidal and bile salts signature and genetic + microbiomic profile combined with detailed clinical-chemical-endocrine phenotype.

E-Ob and L-Ob was found in **55 (32F/23M)** and **184 (83F/101M)** subjects, respectively, in 2 F patients there were no data of the age of the obesity onset.

Conclusions Irrespective of the time of obesity onset there were no differences in the clinical phenotype and degree of the obesity. **Higher activity of liver enzymes** and **higher value of HbA1c** in children with late-onset obesity, in whom overweight mostly starts at the time of overlapping *adrenarche* & adiposity rebound, indicate the tendency to develop the metabolic syndrome and T2D.

Results

	E-Ob (n=55)		L-Ob (n=184)		p
	mean	SD	mean	SD	
Clinical phenotype of study groups					
Age V0 [years]	11.8	2.2	12.5	2.3	NS
Weight V0 [kg]	74.0	20.2	77.2	20.1	NS
Height V0 [cm]	154.0	11.0	156.4	13.5	NS
hSDS V0	0.7	1.1	0.5	1.1	NS
BMI V0	30.8	5.8	31.0	4.7	NS
Z-score BMI IOTF V0	2.8	0.5	2.8	0.4	NS
Waist V0 [cm]	90.1	12.4	91.3	10.4	NS
Hip V0 [cm]	103.1	13.4	104.3	12.1	NS
Waist-to-hip ratio V0	0.9	0.1	0.9	0.1	NS
Waist-to-height ratio V0	0.6	0.1	0.6	0.0	NS
BP SYS V0 [mmHg]	124	14	123	14	NS
BP DIAS V0 [mmHg]	77	11	78	11	NS
HRV0 [/min]	89	14	87	12	NS
Acanthosis nigricans [%]	50.9	-	42.2	-	NS

Body composition*					
FAT [kg]	30.9	13.1	31.2	10.6	NS
FAT%	41.0	7.7	40.1	7.1	NS
FFM [kg]	43.4	10.4	46.1	12.4	NS
FFM%	59.6	7.7	60.2	6.9	NS
TBW [kg]	31.8	7.7	33.9	9.2	NS
TBW%	43.7	5.7	44.1	4.9	NS
Liver steatosis (US) [%]	38.2	-	49.5	-	NS

Questionnaire data					
Mother's BMI	29.9	6.8	30.6	6.9	NS
Mother's Ob[%] (pregnancy)	50.9	-	50.8	-	NS
Father's BMI	37.4	44.7	30.3	6.2	NS
GA/Hbd [wk]	39.0	1.6	38.9	1.7	NS
C-section delivery [%]	54.5	-	47.3	-	NS
Birth weight [g]	3396	537	3247	565	NS
Breast feeding [mo]	11.5	12.3	9.9	11.1	NS
ATB 1st year of life [%]	50	-	52.6	-	NS
Physical activity hrs/wk	3.4	2.8	3.4	3.0	NS
Moderate economic status [%]	76.4	-	70.1	-	NS

Biochemical phenotype of study groups**					
PLT [10 ³ /uL]	299.6	87.6	296.5	76.1	NS
GLU 0' [mg/dl]	91.1	6.2	92.6	8.9	NS
INS 0' [uIU/mL]	24.0	16.4	23.5	14.5	NS
INS/GLU (>0.3)	0.26	0.18	0.25	0.13	NS
HOMA-IR	5.4	3.7	5.5	4.3	NS
HbA1c [%]	5.3	0.3	5.5	0.4	0.007
HbA1c >5.7% [%]	7.3	-	21.2	-	0.03
GLU 120' [mg/dl]	107.8	23.5	111.7	28.7	NS
INS 120' [uIU/mL]	125.5	100.0	113.9	86.1	NS
Tchol [mg/dl]	162.7	23.8	164.0	29.8	NS
HDL-chol [mg/dl]	45.9	7.4	46.5	9.1	NS
TG [mg/dl]	100.3	45.7	101.2	48.4	NS
TSH [uIU/mL]	3.3	1.4	3.2	1.6	NS
fT4 [ng/dL]	1.1	0.2	1.1	0.2	NS
Cortisol [uug/dL]	11.5	4.7	11.2	4.7	NS
ALT [U/L]	21.6	9.1	27.5	25.2	0.009
ALT > norms	5.4	-	13.0	-	NS
AST [U/L]	23.1	6.4	27.2	22.5	0.019
GGTP [U/L]	15.1	4.9	17.9	9.7	0.007
Ferritin [uug/l]	50.5	40.2	49.2	30.6	NS
Uric acid (UA) [mg/dl]	5.5	1.1	5.4	1.3	NS
Creatinine [mg/dl]	0.56	0.11	0.54	0.12	NS

Legend: V0- 1st visit before intervention, z-score BMI IOTF-BMI cut-offs based on International Obesity Task Force; BP SYS – systolic blood pressure; BP DIAS – diastolic blood pressure; HR – heart rate; FFM – fat-free mass; TBW – total body water; Ob- obesity; GA- gestational age; ATB – antibiotics; PLT - ; GLU – glucose; INS- insulin; Tchol – total cholesterol; TG – triglycerides; * - based on bioelectrical impedance analysis (BIA) using segmental body composition analyzer; ** -morning fasting venous blood samples

