



LETTER TO THE EDITOR

Role of socio-economic status in observational studies: A study model on non-alcoholic steato-hepatitis (NASH)



In spite of a great deal of available literature, little is known about the determinants of pediatric metabolic diseases and their long term consequences. Diet composition is only one of the players in the fields, since other factors have been described to have a key role in the development of these conditions, such as genetic background, early epi-genetic events and lifestyle and environmental variables [1–3].

To explore the role of the major individual variables potentially related to disease development, we have evaluated the independent role of environmental and biologic risk factors in the development of non-alcoholic steato-hepatitis (NASH), considered as a major complications of pediatric obesity and its long-term clinical sequelae. Within this analysis the separated role of socioeconomic status (SES) has been considered.

Within a monocentric observational study, 182 obese/overweight children, 102 males (56%), with biopsy proven nonalcoholic fatty liver (NAFL) were enrolled at the Liver Unit, “Bambino Gesù” Children’s Hospital, Rome, Italy from June 2013 to December 2015. The prevalence of NASH/not NASH (=NAFL), diagnosed by a Steatosis, Activity and Fibrosis (SAF) score and FLIP algorithm [4], was evaluated against simple and validated markers of genetics (PNPLA3-GG genotype), parental obesity (yes/not, either one or both), jobs (coded as proxy of SES according to categories of Italian National Institute of Statistics [ISTAT] classification [5]), gestational age (≥ 37 wks vs < 37 wks), weight at birth (≤ 10 th percentile, $> 10 < 90$ th percentile, ≥ 90 th percentile), breastfeeding (formula fed, breastfed for less than 50% feedings after the first two weeks), and fructose consumption, as indicator of junk food consumption (using Italian Food composition Tables [INRAN-CREA] after recording food frequency questionnaires [6,7]). Binary logistic regressions were used to analyze data. Moreover, the attributable risk (AR, measuring the impact of any single factor against another/others) was calculated.

The results show that the 67.6% (123) of children were obese, the remaining 32.4% (59) overweight. Within the whole population 47.8% (87) of children show at least one

parent with obesity, 26.9% (49) were born preterm, 20.3% (37) were small gestational age (SGA) and 45.6% (83) were breastfed (BF, average duration 8, range 4–12, months). No mother was diagnosed with gestational diabetes.

In the logistic regression for familial SES, 55% (100) had a low SES while 45% (82) a medium–high SES. In this model, SES is inversely associated with the BMI of children (OR = 1.55, 95% CI 1.23–1.97; $p = 0.002$) and familial obesity (OR = 3.83, 95% CI 1.27, 5.78; $p = 0.017$), thus demonstrating that the socio-economics background is a strong determinant of an obesogenic environment.

Within a logistic regression model a higher SES stands as a protective factor for the development of NASH (OR = 0.16, 95% CI 0.11–0.41; $p = 0.0001$). Also, the PNPLA3-GG genotype, parental obesity, birth weight (small for gestational age, SGA, compared to the Adequate GA condition), and early and subsequent feeding (non-breastfed and fructose consumption) are factors predisposing as well to NASH, although in a less significant fashion (data not shown).

Finally, we calculated the SES attributable risk (AR) compared to one or more variables, significantly associated with NASH at bivariate analysis (Table 1).

Considering the AR resulting from matching SES against the other variables SES conditions alone may carry 41% of the attributable risk to develop NASH from NAFL in pediatric overweight and obese patients.

Our observations strongly support that the socio-economic context itself is a main determinant of the

Table 1 AR of SES against variables significantly associated with NASH at bivariate analyses.

	p	AR
SES vs parental obesity	0.03	0.21 (21%)
SES vs parental obesity + genetics	0.002	0.23 (23%)
SES vs parental obesity + genetics + Formula feeding + fructose intake	0.001	0.41 (41%)

development of metabolic consequences of childhood overweight and obesity, in agreement with the WHO vision of life course approach in the prevention of chronic diseases [7]. These observations are consistent with our recent report of an inverse correlation between childhood overweight and obesity and the Gross Domestic Product at the regional level in Italy [8].

Presently, economics is poorly integrated with the leading trends in nutrition science or practice, and within nutritional trials (where we base our evidence-based conclusions) socioeconomic factors are even not considered at all, although it has been recognized by epidemiologists that it is plausible that may be at the root of health problems [2]. Accordingly, poor and unbalanced dietary habits may be a proxy and/or a correlate of different paths through which social factors may operate on health (for instance, through lifestyle and environment).

Promotion of breast-feeding is a first intervention to reduce the social inequalities [9]. This practice is free, accessible to everyone and has a doubtless life-long preventive effect toward obesity and metabolic diseases, including NASH [10]. Disentangling breastfeeding and its effects from socioeconomic determinants is indeed hard [9]. It is afterward responsibility of Governments to ensure the access to healthcare Institutions and appropriate education/instruction to infants and children, and related caregivers. Since the higher cost of healthy diets may significantly contribute to highlight socioeconomic disparities in diet quality, disentangling lifestyle-associated dietary models that are at the same time feasible and acceptable as for taste and traditional backgrounds represents now a priority to counteract social inequalities in either well-developed and developed Countries [11,12].

The interplay between dietary patterns, health status and socioeconomic conditions should be evaluated also on a transgenerational basis to counteract negative epigenetic effects, considering in particular ethnic and immigrant groups within well-developed countries, and poorer populations living in countryside versus those moved to richest centers in transition countries [13]. The economical burden expected in these groups following the consequences of early onset chronic degenerative disorders could more advantageously counteracted by economical and cultural interventions promoting healthy lifestyles in the most disadvantaged young generations, thus improving benefits for the whole population while reducing costs for the chronic disabilities.

Finally, the need to respect sustainability should be considered too. In a broader sense, “interventions on dietary habits require considerations on food security, economic and environmental sustainability, and a broad meaning of wellbeing which includes, but also goes beyond, health effects” [14].

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