Environmental and genetic and factors in pediatric multiple sclerosis (PEDIGREE Study)

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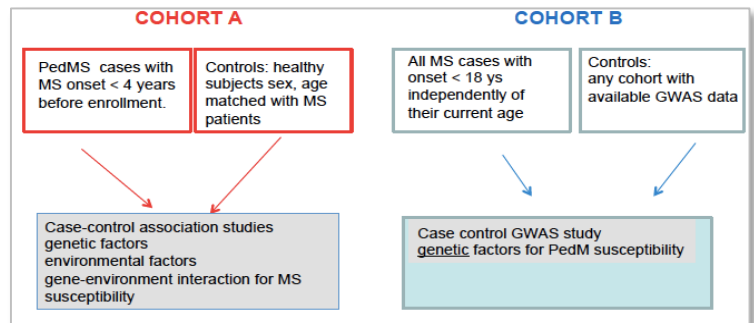
BACKGROUND

Pediatric multiple sclerosis (pedMS) is a privileged condition for exploring the mechanisms involved in MS development because children are close to the exposure to environmental factors with a possible causative role.

AIMS OF THE STUDY

PRIMARY OBJECTIVES

1. To evaluate the exposure to environmental factors (eg., exposure to passive/active cigarette smoking, sunlight, vitamin D supplementation, early life nutrition, increased body mass index, poor physical activity, childhood infections, and vaccinations) and risk to develop MS (Cohort A)
2. To identify genetic risk factors associated with MS, with the objective:
   i) to measure the genetic burden of pediatric-onset,
   ii) to identify genetic variants associated with the risk of PedMS by means of case-control association study at Genome-wide and mitochondrial DNA levels,
   iii) to evaluate the familial aggregation of the disease in PedMS (Cohort A and B)

SECONDARY OBJECTIVES

1. To investigate on gene-environment interactions associated with PedMS (Cohort A)
2. To investigate on the role of gut microbiota in PedMS Cohort A)

COHORT A

| PedMS cases with MS onset < 4 years before enrollment. | Controls: healthy subjects sex, age matched with MS patients |

Case-control association studies genetic factors environmental factors gene-environment interaction for MS susceptibility

COHORT B

| All MS cases with onset < 18 ys independently of their current age | Controls: any cohort with available GWAS data |

Case control GWAS study genetic factors for PedM susceptibility

TIMELINE and MAIN STUDY PHASES:

- **February 2018:** approval by FISM and fund assigment
- **June 2018:** EC clearance obtained for Coordinating Centre
- **June 2018:** EC submission to local ECs of the 35 MS Centres
- invited to participate to the study
- **February -May 2020**: stop related to COVID-19 pandemia
- **March 2020**: translation of the Questionnaire by Waubant et al.
- **July 2020:** EC clearance obtained from 24 of the Centres
- **August – October 2020**: adaptation of Q. by Waubant et al.

PEDIGREE-Q has been adapted to our population in a pilot study involving 67 pediatric subjects and 66 parents *[Pilotto et al.: paper in preparation)*

Methodology: The pilot study was conducted to test acceptability, feasibility, test-retest reliability and relevance by using reference methodology *[Pugliatti et al. 2012]* and involved a number of Italian MS Centres (Ferrara, Pavia, Gallarate, Milan (V. Buzzi Hospital) and Novara. While filling out the questionnaire, the participants were asked to evaluate, in a separate ad hoc and structured form, (i) <u>acceptability</u>, (ii) <u>feasibility</u> and (iii) <u>relevance</u> of question

acceptability and feasibility of the questionnaire

		Questions about Child		Questions about Parents	
		Acceptability	Feasibility	Acceptability	Feasibility
Fair agreement[1]	<40%	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Moderate agreement	40-59%	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Substantial agreement	60-79%	0 (0%)	1 (1.05%)	1 (0.6%)	10 (6%)
Almost perfect agreement	80-100%	95 (100%)	95 (100%)	165 (99.4%)	155 (94%)

changes of PEDIGREE Q after the pilot study

	Questions about Child	Questions about Parents
Number of Questions in Waubant Q[2]	95	166
Adapted/modified Questions to Italian Population	31 (32.6%)	58 (35%)
Deleted Questions	17 (18%)	13 (7.8%)
Added Questions	9 (9.5%)	1 (0.6%)
Number of questions in Pedigree Q	78*	118*

Conclusions:

- the study is ongoing
- a questionnaire has been developed and tested, showing a good acceptabiity,feasibility and relevance
- the questionnaire could be used in other studies to explore environmental factors in MS