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Seasonal variation of semen parameters correlates with environmental temperature and air pollution: A big data analysis over 6 years☆

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ABSTRACT

Background: Male fertility is progressively declining in many developed countries, but the relationship between male infertility and environmental factors is still unclear.
Objectives: To assess the influence of environmental temperature and air pollution on semen parameters, using a big-data approach.
Methods: A big data analysis of parameters related to 5131 men, living in a province of Northern Italy and undergoing semen analyses between January 2010 and March 2016 was performed. Ambient temperature was recorded on the day of analysis and the 90 days prior to the analysis and the average value of particulate matter (PM) and NO2 in the year of the test. All data were acquired by geocoding patients residential address. A data warehouse containing 990,904,591 data was generated and analysed by multiple regressions.
Results: 5573 semen analyses were collected. Both maximum and minimum temperatures registered on the day of collection were inversely related to total sperm number ($p < .001$), non-progressive motility (NPrM) ($p < .005$) and normal forms ($p < .001$). Results were confirmed considering temperature in the 30 and 60 days before collection, but not in the 90 days before collection. Total sperm number was lower in summer/autumn ($p < .001$) and was inversely related with daylight duration ($p < .001$). PM10 and PM2.5 were inversely related to PrM ($p < .001$ and $p < .005$) and abnormal forms ($p < .001$).
Conclusions: This is the first evaluation of the relationship between male fertility-related parameters and environment using a big-data approach. A seasonal change in semen parameters was found, with a fluctuation related to both temperature and daylight duration. A negative correlation between air pollution and semen quality is suggested. Such seasonal and environmental associations should be considered when assessing changes of male fertility-related parameters over time.

1. Introduction

A decline in sperm concentration of about 50% over the last 50 years was proposed for the first time in 1992 (Carlsen et al., 1992). However, this issue remains controversial and several authors highlighted the limits of this finding, from the lack of inference evaluation (Lerchl and Nieschlag, 1996; Olsen et al., 1995) to the low validity of statistical methods (Brake and Krause, 1992; Farrow, 1994), to the bias due to the heterogeneity in study population (Bromwich et al., 1994). Recently, a reanalysis of these data, considering the presence of possible confounding factors, e.g.

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Abbreviations

FSH	follicle-stimulating hormone
NPrM	non-progressive motility
OCSAE	Ospedale Civile Sant'Agostino Estense
PCA	Principal Component Analysis
PM	particulate matter
PrM	progressive motility
WHO	World Health Organization

duration of abstinence time, patients' age and differences among specimen collection methods, confirmed the significant decline in sperm concentration only in some countries (Swan et al., 1997, 2000). In particular, developed countries, such as United States, Europe and Australia, showed a significant sperm count decline, whereas non-developed countries did not observe this impairment (Swan et al., 1997, 2000). This is further confirmed in a large meta-regression analysis, which detects a significant impairment of sperm counts in North America, Europe, Australia and New Zealand, between 1973 and 2011 (Levine et al., 2017). Moreover, several observational trials suggested geographical differences in sperm concentrations in Europe and North America (Joffe, 2003). These studies showed a total sperm number higher in New York and Finland, when compared to California, Denmark and Britain (Joffe, 2003). Several hypotheses have been proposed to explain this geographical variation in semen parameters. Among them, the role of environmental temperatures was considered, although not completely confirmed. Animal models suggest a negative effect of high environmental temperatures on sperm quality, causing different degrees of infertility (Maya-Soriano et al., 2015). On the contrary, large studies evaluating the role of environmental temperature on human spermatogenesis are missing, although the detrimental role of high temperature at genital level is well demonstrated. Recently, we suggested a negative correlation between environmental temperature and semen quantity-related parameters, performing a retrospective, observational pilot study with a limited sample size and a short time-frame interval in a defined geographical area in the North of Italy (Santi et al., 2016).

Environmental parameters to be considered enclose chemicals, endocrine disruptors and complex mixtures of substances, which are potentially able to influence spermatogenesis (Hammoud et al., 2010). This influence should be further evaluated considering the potential effect of chemicals on sperm epigenetic changes (Leenen et al., 2016; Santi et al., 2017). Although these substances can be found in polluted air, the relationship between male infertility and pollution remains controversial (Carlsen et al., 1992; Forti and Serio, 1993; Jensen et al., 2002). Animal models confirm the detrimental role of environmental pollution on male reproduction (Watanabe and Oonuki, 1999), but this issue remains largely debated in humans. In particular, it is accepted that human spermatogenesis is impaired by exposure to environmental chemicals during fetal life (Sharpe and Skakkebaek, 1993) or adulthood (Sharpe, 2010). However, the mechanism by which these air pollutants could affect human spermatogenesis is completely unclear. Only few studies suggested a correlation between toxins in the air and sperm quality in humans (De Rosa et al., 2003; Hovatta et al., 1998; Mendiola et al., 2014; Viskum et al., 1999). Our previous pilot study did not demonstrate any significant correlation between particulate matter (PM) and semen parameters (Santi et al., 2016). PM represents the most used and reliable tool to evaluate air pollution, and it is useful to quantify air composition, measuring different substances, such as carbon monoxide, nitrous dioxide, sulphur dioxide, ozone and lead burden (Santi et al., 2016).

With this in mind, the aim of this study is the evaluation of the changes of semen analysis-related parameters in a wide time-frame interval, considering the population of a Northern Italy region referring to a single centre. In particular, we aim at evaluating the influence of environmental parameters, such as temperature and air pollution on human male fertility, using a real-world, big data approach.

2. Materials & methods

A longitudinal, observational, retrospective, real-world, big data trial was carried out in the "Ospedale Civile Sant'Agostino Estense" (OCSAE). The hospital is located in the province of Modena (Emilia-Romagna region), which comprehends 2689 km^2 and 701,642 inhabitants (updated to 2015) in Northern Italy. In general, the population of the province shows a mean age of 44.3 years with a birth rate of 8.5 per thousand inhabitants and a mortality rate of 10.4 per thousand inhabitants (old age index of 156.28 years) (http://www.urbistat.it).

Fig. 1 describes the study design, from data source, through the number of samples included in the data warehouse and the final data integration, analysis and evaluation.

2.1. Subjects

All the laboratory examinations performed at OCSAE in the central laboratory of the Department of Clinical Pathology were included in a large database, enclosing 990,904,591 records (Fig. 1). This data consisted only of biochemical and hormonal parameters. Thus, no further clinical information is available, apart from the age and the residential address of the subject. From this large database, all semen analyses conducted from January 2010 to March 2016 were exported.

The study design did not foresee any inclusion/exclusion criteria for enrolment. The database was formed by the entirety of all semen analysis results produced by the laboratory in the considered time period. Thus, patients enrolled in the study were most probably both infertile and fertile men, undergoing seminal examinations as requested the treating physicians, who could be the general practitioners or a specialist (presumably urologist, endocrinologist or gynaecologist), according to the rules of the National

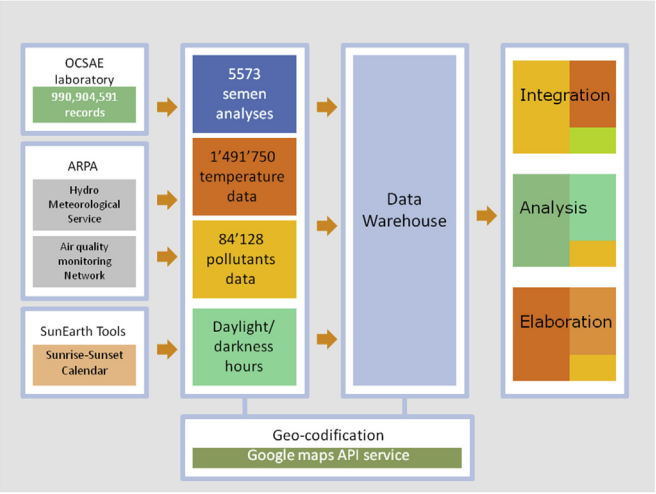

Fig. 1. Study design.