



## Platinum Priority – Editorial

Referring to the article published on pp. 482–490 of this issue

# Hypospadias increased prevalence in Surveillance Systems for Birth Defects is observed: Next to climate change are we going towards a human fertility alteration?

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In this issue of *European Urology*, Yu et al [1] analyze surveillance systems for birth defects in 27 countries. The authors' aims were to analyze the prevalence and trends regarding hypospadias over a long-term period of 31 yr in a large population. They gathered data from 27 countries participating in the World Health Organization–affiliated International Clearinghouse for Birth Defects Surveillance and Research. Of the 27 participating programs included, 13 were from European countries, five from South America, six from North America, and one each from New Zealand, Australia, and Iran.

In total, 36 127 500 births were reported, with 74 814 hypospadias cases. For all programs combined, the total prevalence of hypospadias was 20.9 cases per 10 000 births (95% confidence interval 19.2–22.6) for the study period of 1980–2010. The prevalence among countries ranged from 2.1 cases per 10 000 births in Argentina to 39.1 cases per 10 000 births in Arkansas, USA. Overall, Latin American countries had relatively lower prevalence compared to other surveillance programs. In Europe the prevalence was highly variable, ranging from 10.6 (France) to 37.4 (Lombardy, Italy) per 10 000 live births.

The authors used Joinpoint trend analysis regression, which is the model most used for population-based analysis, to determine whether the prevalence evolved over the years among the participating programs [2].

The authors report that the international total prevalence increased by a factor of 1.6 during the study period, equivalent to 0.25 cases per 10 000 births per year ( $p=0.001$ ), with clear evolution over time. The increase was 0.19 cases per 10 000 births year between 1980 and 1996, while the period 1999–2010 saw an increase of

0.34 cases per year per 10 000 births. Only 12 of the 27 programs reported the severity of the hypospadias in more than 80% of cases, limiting the possibility to determine statistically significant differences between the types. Some 62.2% of the cases had distal hypospadias, 20.1% had mid-penile hypospadias, 4.5% had proximal hypospadias, and 13.2% had an unspecified degree of severity. The authors conclude that despite changes in clinical practice and associated registry reports over time in some countries, the consistency observed for the increasing trends for hypospadias prevalence across the international surveillance programs suggests that the total prevalence of this condition is increasing in many countries.

Whether hypospadias, one of the most common congenital malformations, has been increasing over the past decades or not is a matter of debate [3]. Some authors report a clear increase in some countries [4], while others claim that there has been no increase but rather a higher detection rate over recent decades [5]. With increasing awareness of climate change and plastic pollution and their possible repercussions for human health, finding an answer to this question appears to be of utmost importance. Plastic, like many environmental pollutants, is recognized as an endocrine disruptor [6]. Endocrine disruptors act as estrogen-like molecules and can cross the placenta membrane during pregnancy. It is believed that they have a potential influence on the formation of the male genitalia [7] and can eventually induce testicular dysgenetic syndrome [8]. Increasing fertility problems, low sperm counts, and male genital malformations over the past decades might be a result of the consequences of human-related environmental modifications.



The population-based report by Yu et al confirms that there seems to have been a real increase in hypospadias over the past decades. The study population is worldwide, demonstrating that the increase is not limited to a few areas. Even if there are some variations in the reporting of data among the centers, the data remain statistically significant: there is an increase in hypospadias prevalence in most parts of the world, as represented by a sample of 27 programs involved in detection of birth defects with a global spread.

It would have been interesting to have more data on hypospadias severity, as it is believed that proximal severe hypospadias is related to genetic conditions, while distal and mild hypospadias could be related to epigenetic factors such as environment and maternal exposure to pollutants [9]. If environmental changes and epigenetic modifications are indeed responsible for an increase in the prevalence of hypospadias worldwide, one would expect a clear increase in distal compared to proximal hypospadias.

In vitro fertilization, older maternal age, and family history are known risk factors for hypospadias [10]. It would be extremely interesting to match this cohort analysis with data regarding mothers and associated anomalies in the children. How old was the mother at the child's birth? Was the pregnancy natural or achieved in vitro? Was there any family history? Were there any associated cryptorchid testicles? What was the birth weight? Answers to such questions would help us to understand better the mechanisms underlying male testicular and genital disorders and might be important in the prevention of concerning increases in male genital and fertility problems.

**Conflicts of interest:** The author has nothing to disclose.

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