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## Do patients with hypospadias and cryptorchidism share a common phenotype? Case–control study of an Italian paediatric population

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### KEYWORDS

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**Abstract** *Objective:* A large number of children affected by hypospadias and undescended testis (UDT) are characterized facially by a large forehead with frontal bossing, telecanthus and broad flat nasal bridge. These traits are classically part of the clinical spectrum of the Opitz-GBBB and other syndromes. The aim of this study was to test the hypothesis that the presence of these features in isolated hypospadias and UDT is not correlated with chromosomal anomalies and/or syndromes, but defines a distinct morphology.

*Patients and methods:* Two hundred patients affected by isolated hypospadias and 100 presenting with a UDT were evaluated for facial biometric indices. An age-matched group of patients was used as control. The parameters inter-pupillary/inner canthal ratio and glabella–nose tip/nasion distance were then calculated.

*Results:* The glabella–nose tip/nasion distance was significantly different between hypospadias and control groups, but was not different between UDT and control groups. There was no difference in inter-pupillary/inner canthal ratio.

*Conclusion:* Children affected by hypospadias and/or UDT frequently present peculiar phenotypic features making it possible to recognize them 'at first glance'. This association needs to be explained in future studies.

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## Introduction

In our daily hospital activity we have the opportunity to see a large number of children affected by hypospadias and undescended testis (UDT). We have noticed how easy it is to identify these children, even before the parents declare the reason for consultation, by their particular facial traits.

They often exhibit a large forehead with frontal bossing, telecanthus and a broad flat nasal bridge. These traits are also part of the clinical spectrum of the Opitz-GBBB [1] and other syndromes, in which hypospadias is one of the main features. In isolated hypospadias, they are somehow different to the features seen in classic Opitz syndrome, and may be observed also in many children with UDT, defining therefore a potentially distinct morphology. The aim of this study was to demonstrate this autonomous association between facial appearance and hypospadias, and discuss its statistical relevance.

## Patients and methods

Two hundred patients affected by hypospadias (Hypo group) and 100 presenting only with an undescended testis (UDT group) were seen at our outpatient department, and all registered, photographed and evaluated for facial biometric indexes. Mean age was 15 months (range: 2–24 months) for the hypospadias group and 11 months for the cryptorchid children (range: 1–24 months). An age-matched group of patients (control) were enlisted from those referring to general pediatricians for routine check up, without specific health problems.

The picture of the child's face was taken from a distance of 1 m, so as to reduce the influence of the focal distance on

the measurement obtained. Informed consent was requested and signed by the parents before taking the pictures.

The following parameters were then calculated by image-processing software: inter-pupillary/inner canthal ratio (IP/ICR) and glabella–nose tip/nasion distance (GNND) (Fig. 1). Median values of each group were compared by a statistical software package (Graph Pad InStat from Graph Pad software Inc., San Diego, CA, USA).

## Results

Scattergram of IP/ICR and GNND values of patients of each group, and results of the statistical analysis are shown in Fig. 2. There were no statistically significant differences in IP/ICR between the three groups. Comparing GNND values, we found a statistically significant difference between Hypo and control groups ( $p < 0.005$ ); this difference was not statistically significant between UDT and control groups ( $p = 0.0771$ ).

## Discussion

Our data show that children affected by hypospadias and/or UDT present with peculiar phenotypic features mainly represented by large forehead with frontal bossing, telecanthus and broad flat nasal bridge. In our series these features were present in up to 87% of hypospadiac patients, 72% of those with UDT and only 24% of the control patients. From the evaluation of facial biometric indexes, the measurement of the IP/ICR does not show any significant difference from controls, while only in the Hypo group does the GNND show a statistically significant difference. Even if typical facial traits are present in most of the patients with

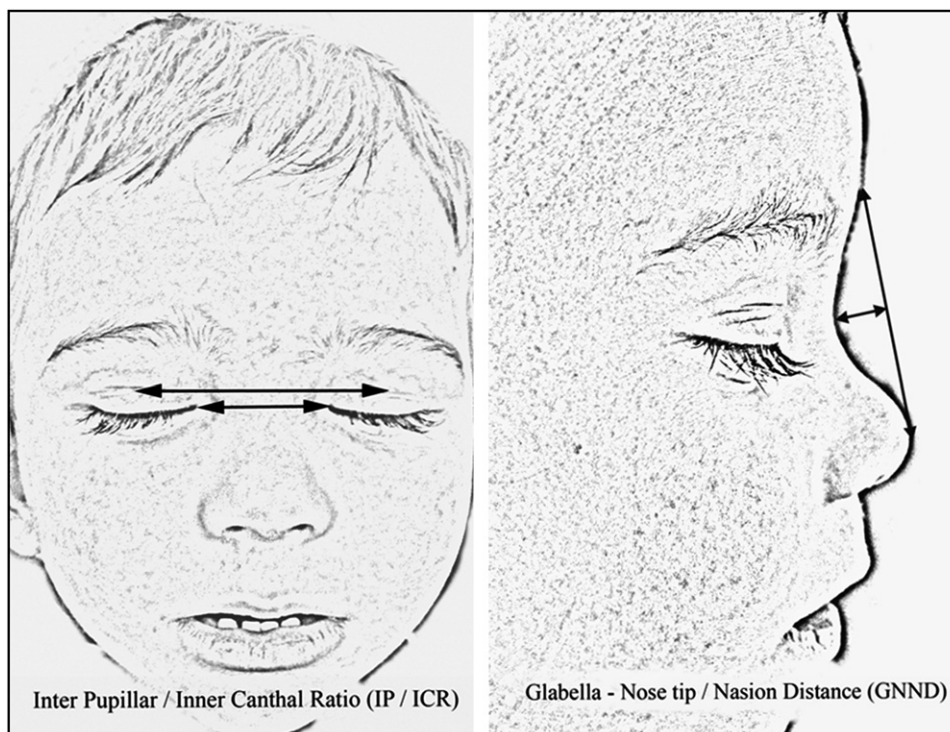


Figure 1 Facial biometric indexes.

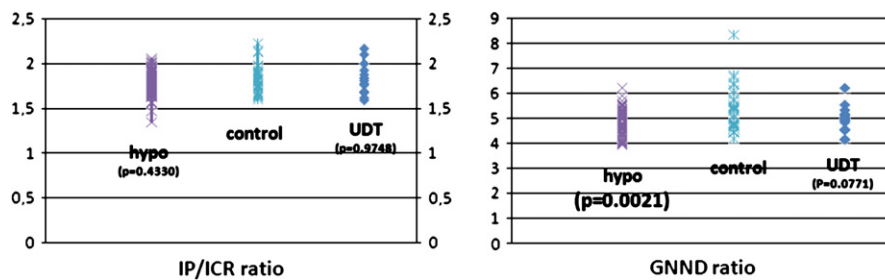


Figure 2 Scattergram showing distribution of population by group and results of statistical analysis.

UDT, there is no statistically significant difference from the control group; the authors believe that these indices probably do not represent the whole aspect of these facial features.

It is worth noting that the frontal squama develops by bone displacement and sutural response [2] as a consequence of encephalic pressure in terms of size, and of the connective brain tensors as the *falx cerebri* in terms of shape [3]. As a result, changes in frontal morphology are secondarily related to brain development, and not to direct local morphogenesis. In terms of development, 'relative larger vault' or 'relative smaller face' means a difference in timing between neurocranium and splanchnocranium growth. In this case, it is possible to hypothesize a reduced rate or delayed onset of facial development. The compression at the nasal base is rather interesting in this perspective, as this area is a borderline structural morphogenetic source in terms of facial development and midfacial/lower facial lengthening during both ontogenesis and evolution [3–8]. We can therefore hypothesize a common ground between hypospadias and facial development, at least during early childhood. Future analysis must be aimed at considering the morphological variation of these traits and the structural correlation with facial size and age.

## Conclusions

Many children with hypospadias (and perhaps UDT) have peculiar facial features whose frequency seems statistically

relevant when compared to a control group. This association needs still to be explained in future studies. Its potential correlation with different specific genetic anomalies is under further evaluation at the present time in our hospital.

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