FOETO-PLACENTAL WEIGHT RELATIONSHIP IN HYPOSPADIAS CHILDREN AND IN NORMAL CHILDREN WITHOUT HYPOSPADIAS - A COMPARATIVE STUDY

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ABSTRACT
Hypospadias is a congenital anomaly occurring in male newborn. It is the abnormal opening of the urethra on the ventral surface of the penis, with or without chordee. It is the result of arrested development of urethra, foreskin and ventral aspect of penis for which the only treatment is surgery. The majority of hypospadias are believed to have a multifactorial etiology. Thus, prevention is imperative. To accomplish this, it is necessary to determine the etiology of hypospadias. The association of growth retardation and hypospadias is well established. In addition to many risk factors, lower birth weight has been associated with hypospadias. Another study found that boys with hypospadias have a lower placental weight than normal boys. Fetal testosterone secretion is under the influence of placental human chorionic gonadotropin during first 14 weeks of gestation. The placental insufficiency may disrupt the supply of nutrients and hCG to the fetus leading to growth retardation and hypospadias. To validate this hypothesis, we analyzed all the male infants born at our hospital with or without hypospadias for fetal growth parameters and collected placentas for detailed evaluation. The specific association of fetal weight and placental weight in hypospadias children and in controls seems to be insignificant.

Key Words: Hypospadias, placenta, foeto-placental ratio, etiology

INTRODUCTION
Hypospadias is the most common congenital anomaly, which occurs in approximately 1 in 250 male births¹. Hypospadias can be defined as an arrest in normal development of urethra, foreskin and ventral aspect of the penis. This results in wide range of abnormalities. Hypospadias is classified depending on the location of the urethral opening². Anterior hypospadias is described as glandular, coronal or distal. Middle hypospadias is along the middle third of the penile shaft. Posterior hypospadias extends through the proximal third of the penile shaft to the perineum and is described as posterior penile, penoscrotal and scrotal or perineal. Chordee or penile curvature is a downward curvature of the penis that typically accompanies the more severe hypospadias³. Formation of external male genitalia is a complex developmental process involving genetic programming, cell differentiation, hormonal signaling, enzyme activity and tissue remodeling. By the end of 4 weeks of gestation, the hind gut and future urogenital system reach the surface of the embryo at the cloacal membrane on the ventral surface. During this indifferent stage up to the eighth week, the cloacal membrane, under the genital tubercle is divided into anal and urogenital membrane. The urogenital membrane is flanked on each side by two genital swellings, forming the urethral groove. At this point, musculanization of the external genitalia commences under the influence of testosterone converted in to 5α –dihydrotestosterone in response to a surge of luteinizing hormone from the pituitary⁴. One of the first signs of musculanization is an increase in the distance between the anus and genital structures. This is followed by elongation of the phallus, formation of penile urethra from the urethral groove beginning from the anus at about 11 weeks and the development of the prepuce⁵. The entire male urethra is formed by dorsal growth into the genital tubercle and ventral growth and fusion of urethral fold⁶. Reports of increasing prevalence of hypospadias have raised questions concerning etiology, treatment and prevention. To date there is no comprehensive understanding of the etiology of hypospadias that can inform primary prevention efforts and improve therapeutics. In some studies it was found that the boys with hypospadias have a lower birth weight, and the placentas collected from their mothers also had less...
weight than the controls, so that placental function can be one of the etiologies of hypospadias\(^4\). In the present study, an attempt is made to study the foeto-placental weight relationship in hypospadias children, which is compared with normal children having same birth weight.

**MATERIALS AND METHODS**

Between July 2008 and June 2010, the database of the neonatal intensive care unit at K. L. E. Hospital, Belgaum indicated that the total number of male births in the center during the study period was 3243. All male newborn delivered in our hospital were examined for hypospadias. Once hypospadias was identified, the neonate was examined in detail to identify other anomalies, weight at birth and gestational age. The placenta were examined after delivery. Adherent clots were removed, placenta were washed thoroughly with water, cord was cut 4 cm from insertion and placenta were weighed. The placenta was collected and examined for placental weight and thickness. Fetus to placental weight ratio was measured as a reference for placental function and intrauterine fetal growth. Statistical significance was analyzed with Student's 't' test and standard error of proportion between two means.

**Results**

During the study period 15 children were born with hypospadias in our hospital. Another 15 children without hypospadias acted as controls. The fetal weight, placental weight and foeto-placental ratio are shown in Table 1. As compared to control group with hypospadias infants, there was no significant difference between fetal weight, placental weight and foeto-placental ratio.

**DISCUSSION**

A detailed report by Baskin suggests a multifactorial etiology of hypospadias fitting a polygenic model\(^5\). Responsible etiologic factors may include one or more of an environmental or other endocrine disruptor; an endocrinopathy, enzymatic or local tissue abnormality and a manifestation of arrested development. The characteristic defect of hypospadias may result from one or more of the following, abnormal androgen production by fetal testes, limited androgen sensitivity in the target tissue of developing external genitalia or premature cessation of androgenic stimulation secondary to premature involution of Leydig cells of the fetal testes\(^5\). Conversion of testosterone to dihydrotestosterone and proper androgen receptor signaling are critical to normal urethral closure. Several studies have found association between hypospadias risk and preterm birth and low birth weight\(^6\). Disturbance of placental function early in pregnancy is a key mechanism underlying both preterm birth or low birth weight and the improper closure of the urethra, because the placenta is the main product of pregnancy hormones in early pregnancy\(^7\). In our study, the fetal weights as well as the placental weights were the key parameters. The specific association of fetal weight and placental weight in hypospadias children and in controls seems to be insignificant. Therefore, in conclusion we can say that there is no relationship between the placental weight and fetal weight in the etiology of hypospadias.

**Table 1: Key parameters of male births with hypospadias and controls**

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Hypospadias</th>
<th>Controls</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fetal Weight in grams</td>
<td>3003.8±191.99</td>
<td>3115.38±384</td>
<td>0.1709*</td>
</tr>
<tr>
<td>Placental Weight in grams</td>
<td>462.3±8.6</td>
<td>461.92±8.0</td>
<td>0.909*</td>
</tr>
<tr>
<td>Foeto-placental Ratio</td>
<td>6.50±0.41</td>
<td>6.74±0.41</td>
<td>0.1438*</td>
</tr>
</tbody>
</table>

*Statistically not significant

**REFERENCES**