

MORPHOLOGICAL AND HISTOPATHOLOGICAL STUDY OF PLACENTA IN CHILDREN WITH AND WITHOUT HYPOSPADIAS

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ABSTRACT

Introduction: Hypospadias is one of the most common congenital anomaly of male external genitalia. It occurs in approximately 1 in 250 new born. Hypospadias can be defined as an abnormal urethral orifice under surface of the penis with or without chordee and with or without dorsal hood. Hypospadias may be an isolated defect or a phenotypical component of a more complex condition such as an intersex state.

Aim: This study aimed to observe and document morphological and histopathological changes of placenta in children with hypospadias and compare with controls.

Materials and Methods: The present study was a case control study and the data base of the labor registries of the hospital indicated that there were total 3243 male births during this period. All examined for presence / absence of hypospadias by attending pediatrician. Hypospadias was detected in 17 male newborns. Control cases comprised of 68 male newborns without hypospadias of similar gestational age and birth weight collected by cluster sampling. The placenta was collected and examined for placental weight, thickness, and histopathology.

Results and Conclusion: Total number of male birth during the study period was 3243, in that 17 children born with hypospadias. The incidence of hypospadias in our hospital was 0.52%, Histopathological study revealed excessive syncytial knots formation, infarction, calcification, thickening of basement membrane, stromal fibrosis, villous oedema, and hemorrhage. But the values were similar in children with hypospadias when compared with controls.

Conclusion: This study shows placental insufficiency is not associated with hypospadias.

KEY WORDS: Hypospadias, Placenta, Infarct, Syncytial Knot.

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INTRODUCTION

Hypospadias is one of the most common congenital anomaly of male external genitalia.

It occurs in approximately 1 in 250 new born [1]. Hypospadias can be defined as an abnormal urethral orifice under surface of the penis with

or without chordee and with or without dorsal hood. Hypospadias may be an isolated defect or a phenotypical component of a more complex condition such as an intersex state. Hypospadias, in boys, defined as an association of three anomalies of the penis: (1) an abnormal ventral opening of the urethral meatus that may be located anywhere from the ventral aspect of the glans penis to the perineum, (2) an abnormal ventral curvature of the penis (chordee), and (3) an abnormal distribution of foreskin with a "hood" present dorsally and deficient foreskin ventrally [2]. The second and third characteristics are not present in all cases. The urethral meatus opens on the glans penis in about 50-75% of cases; these are categorized as 1st degree hypospadias. When urethra opens on the shaft is considered as 2nd degree hypospadias and the urethra opens on the perineum is 3rd degree hypospadias [3]. Hypospadias is a result of arrested development of the urethra foreskin, and ventral surface of the penis where the urethral opening may be anywhere along the shaft, within the scrotum, or in the perineum. The only treatment is surgery. 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. Fetal testosterone secretion is under the influence of placental hcG during first 14 weeks of gestation. Chorionic gonadotropin stimulates fetal testicular testosterone secretion that is maximum at approximately the same time that maximal level of HCG is attained. Thus, at a critical time in sexual differentiation of the male fetus HCG enters fetal plasma from syncytio trophoblast; acts as an LH surrogate and stimulate replication of testicular Ley dig cells and testosterone synthesis to promote male sexual differentiation.

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 hypospadias for fetal growth parameters, and collected placenta for detailed evaluation .

Objectives: To observe and document the morphological and histopathological changes of

placenta in children with hypospadias and compare with controls.

MATERIALS AND METHODS

The present study was a case control study. The data base of the labour registries in our hospital indicated that there were total 3243 male births during this period. All examined for presence /absence of hypospadias by attending pediatrician. Hypospadias was detected in 17 male newborns. Control cases comprised of 68 male newborns without hypospadias of similar gestational age and birth weight collected by cluster sampling. Once hypospadias was identified, the neonate was examined in detail to identify other anomalies, weight at birth, and gestational age. The placenta was collected and examined for placental weight, thickness, placental histopathology and cord information. Fetus to placental weight ratio was measured as a reference for placental function and intrauterine fetal growth. The placenta of these controls was also subjected to detailed evaluation and examination.

Data was compiled and analyzed by descriptive analysis; comparison of risk factors was done using student t test. P value <0.05 was considered as significant.

RESULTS

Total number of male birth during the study period was 3243, in that 17 children born with hypospadias. The incidence of hypospadias in our hospital was 0.52%.

Table 1: Comparison of fetal demographic factors associated with hypospadias.

	Hypospadias (n=17)	Controls (n=68)	P-value
Gestational age (week)	38.64 ± 0.99	38.37 ± 1.14	0.96
Birth weight (kg)	2.96 ± 0.19	3.01 ± 0.17	0.11
Placental weight (gm)	462.31 ± 8.56	461.92 ± 8.04	0.9
Placental thickness (cm)	2.08 ± 0.27	2.00 ± 0.00	0.32
Feto-placental ratio	6.53 ± 0.40	6.74 ± 0.42	0.16

P-value <0.05 is considered as significant

Table 1. Showing the fetal demographic factors associated with hypospadias. In this study the gestational age was similar in hypospadias

(38.64±0.99 weeks) when compared with controls (38.37±1.14weeks). Birth weight in children with hypospadias was (2.96±0.19kg), when compared with controls (3.01±0.17kg). There was no significant difference in placental weight in children with hypospadias (462.31±8.56gm) when compared with controls (461.92±8.04gm). Placental thickness was similar in children with hypospadias (2.08±0.27cm) when compared with controls (2.00±0.00cm). There was no significant difference in placental volume in children with hypospadias (362.65±14.14cc) when compared with controls (364.22±17.17cc). Percentage of infarct in the total volume of placenta was similar in both the groups (3.45±0.23 vs3.48±0.30,P-0.81). Feto placental ratio was not higher in children with hypospadias (6.53±0.40) when compared to controls (6.74±0.42). There was no significant difference in length of umbilical cord in children with hypospadias vs controls (58.31±2.52vs56.85±2.91,P-0.18).

Characteristics of placenta: Gross pathological findings of placentas in children with hypospadias and in controls are shown in Table 2. Gross pathological study revealed infarction and calcification. Infarction was present in 11 placentae of children with hypospadias (64%) and in 45 placentae (66%) of controls. Mild infarction was present in 08 placentae of hypospadias children (47%), and 33 in controls (48%). Moderate infarction was present in 03 placentae of hypospadias children (17%) and 12 in controls (17%).severe infarction was absent in both the groups (Table 3). Calcification was present in 03 placentae of hypospadias children (17%) where as it was present in 12 placentae in controls (17%) (Table3).Placental membrane did not show chorioamnionitis, amnion nodosum, squamous metaplasia, or calcification in both the groups.

Table 2: Gross pathological findings of placenta.

Infarcts	Hypospadias (n-17)	Controls (n-68)
Absent	06 (35%)	23 (33%)
Mild	08 (47%)	33 (48%)
Moderate	03 (17%)	12 (19%)
Severe	Nil	Nil
Calcification	03 (17%)	12 (17%)

Histopathological findings of placentae in children with hypospadias and in controls are shown in (Table 3).

Table 3: Histopathological findings of placenta.

	Hypospadias (n-17)	Controls (n-68)
Infarction (mild to moderate)	11 (64%)	45 (66%)
Excessive syncytial knots	10 (58%)	41 (60%)
Calcification	03 (17%)	03 (17%)
Thickening of basement membrane	04 (23%)	18 (26%)
Stromalfibrosis	0	0
Villous oedema	0	0
Haemorrhage	06 (35%)	25 (36%)

Histopathological study revealed excessive syncytial knots formation, infarction, calcification, thickening of basement membrane, stromal fibrosis, villous oedema, and hemorrhage. Infarcts were present in 11 placentas in hypospadias children and in 45 placentae in controls .The % of mild to moderate amount of infarction in placentae of hypospadias children was 64% and in control group was 66%. Excessive syncytial knots were present in 58% of placentae in hypospadias where as 60% in controls.17% of placentae from both the group had calcification. Stromal fibrosis and villous oedema was absent in both the groups.

DISCUSSION

Many authors have suggested that disturbance of placental function early in pregnancy is the key mechanism underlying both preterm birth/ low birth weight and the improper closure of the urethra, because the placenta is the main producer of pregnancy hormones in early pregnancy and is thus instrumental in the differentiation and development of the fetal organs [4-6]. This study could not find an association between hypospadias risk and preterm birth (<37 weeks gestation) and/or being small for gestational age (<10th percentile) because in this study all the children born with hypospadias were normal birth weight (>2.8 kg) and all of them were term birth (>39 weeks). It is well known that in normal, preterm and term infants there is a direct relation between birth weight and weight of placenta [7]. In this study, since all the children born with a normal birth

weight, there was no significant association between birth weight and placental weight and all placentae were of normal weight. At term, the placenta is approximately 3cm thick and measures 15-25cm diameter [8]. Placental thickness is closely related to fetal well being and may be a key factor in perinatal outcome. In this study, all the placentae were of normal thickness because none of the children in the study group were low birth weight. Ultrasonographic study of placental volume found that, placental volume was directly proportional to the birth weight of the babies [9]. However, there is limited information on the relationship between intrauterine placental volume and birth weight [10]. In this study all the children born with normal birth weight and placentae were in normal weight hence volume of placenta in children with hypospadias was similar with the control on comparison.

The ratio of placental weight to birth weight is described as a marker of fetal growth. The correlation of birth weight and placental size is to be expected as both placental weight and size are known to increase as birth weight increases [11]. In this study the feto-placental ratio in hypospadias children was not found to be increased in comparison with the controls.

Zeek and Assali, 1952, defined placental infarction as a zone of ischemic necrosis of a group of villi due to complete interference with their blood supply in the deciduas or in the local state by thrombosis of a spiral arteriole or a retroplacental hemorrhage [12]. The incidence of placental infarction was found in 25% of normal placentae [13]. In this study, percentage of placental infarction was similar when compared with the controls. Macroscopically visible calcification of the placenta is by means uncommon and may be quite extensive. The incidence of gross placental calcification, of the type detectable by a pathologist, has varied in different studies from 14 to 37% [14]. The incidence in Fox own experience being approximately 19%. In this study, few placentae had calcification and the percentage of calcification in children with hypospadias (17%) was similar when compared with controls (17%) and calcification was found in placentae of primigravid mothers as well. Previous studies

indicate that an excess of syncytial knots is unlikely to be a direct response to placental ischaemia, maternal pre-eclampsia, idiopathic IUGR and to a lesser extent, maternal diabetes mellitus [15]. In this study, the total number of syncytial knots was similar when compared with the controls. A striking increase in proportion of villi with unduly thick trophoblastic basement membrane is a common feature of placentae from women with pre-eclampsia or essential hypertension [16]. In this study, the number of thickenings of basement membrane in placentas of hypospadias children, were similar to that of controls on comparison.

CONCLUSION

Evidence shows that the prevalence of hypospadias has increased from 1970s up to the present in Europe and probably in the United States. There has been some evidence that the incidence of hypospadias around the world has been increasing in recent decades. Incidence of hypospadias in India is not clear. In our sample the incidence of hypospadias was 0.52%. The prevalence of hypospadias recorded at birth may underestimate the true prevalence because some patients are not diagnosed until later in life when the foreskin is retracted. This study recommends that there is a need for uniform guidelines for all registries to follow in diagnosing hypospadias, in order to avoid under ascertainment or over – ascertainment.

Several studies have found reduced placental function as underlying etiology for low birth weight and hypospadias. In the present study all the children born with hypospadias were of normal birth weight. Fetal factors are gestational age, birth weight, placental weight, Feto-placental ratio. These factors were not significantly associated with hypospadias. And there were no morphological and histopathological changes of placenta in children with hypospadias when compared with controls. This study shows placental insufficiency is not associated with hypospadias in normal birth weight children.

Increasing incidence of hypospadias is not only a health-care issue but also a social concern, and financial burden both to the healthcare providers and the parents. The only treatment recommended for hypospadias is a surgical

repair, hence the need for more number of well trained pediatric and urology surgeons. Severe hypospadias can present as a case of ambiguous genitalia with serious and potentially lifelong consequences. Genetic males with hypospadias and wrongly assigned as females in neonatal period and infancy, may need to be reassigned as males and a number of other changes also need to be made including change in birth records, surgery for hypospadias, psychological support, and sometimes even change in address. Surgery in childhood is associated with psychological trauma in children, hence the need for psychosexual counseling and support. Psychosocial support both in home and school need to be made. This is an additional financial burden both for the family and the society. Various studies have tried to elucidate maternal factors responsible for hypospadias. But conflicting evidence exists, the changes in environmental factors, genetic factors, hormonal levels during pregnancy has been generally regarded as the most possible cause for genital defects including hypospadias. These factors have to be considered further to establish the etiology of hypospadias.

Conflicts of Interests: None

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