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Trends and predictors of incidence of hypospadias in a tertiary hospital in South Africa

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Abstract

Background Hypospadias is a penile congenital abnormality characterized by an ectopic urethral opening, ventral curvature and incomplete foreskin closure with a dorsal hooded prepuce. Management of the outcome demands high cost. The aim of this study was to determine the trends and predictors of hypospadias among babies born at Charlotte Maxeke Johannesburg Academic Hospital between 01 January 2014 and 31 December 2016.

Methods Mothers' files from the transfer unit of the labour ward were reviewed. A case–control study compared boys with hypospadias and those without born approximately at the same time. Data were retrospectively collected on data collection forms. EpiData version 3.1 and STATA version 15.1 were used for statistical analysis. The Mantel Haenszel method determined combined odds ratios for hypospadias outcome on boys whose mothers were exposed to certain conditions versus boys of unexposed mothers. Woolf's method was used to compute confidence intervals of the odds ratios. Logistic regression analysis was used to assess the independent contributing maternal factors to the risk of hypospadias.

Results Records of 221 male babies were collected of which 73 were cases and 148 controls in the ratio of 1:2. Hypospadias was more frequent in boys born by Caesarean Section ($p < 0.001$), those with low birth weight ($p < 0.001$) and those small for gestational age ($p < 0.002$). Alcohol use (odds ratio 3.1), smoking (odds ratio 1.54), herbal use (odds ratio 2.05), medical history (odds ratio 2.8), multiple pregnancies (odds ratio 1.69) and maternal congenital abnormalities (odds ratio 3.03) indicated an increased risk of hypospadias. Surgical history (odds ratio 1.29), pre-natal vaccination (odds ratio 0.92), employment (odds ratio 0.85), and education (odds ratio 0.48) were not associated with the risk of hypospadias.

Conclusions Mothers older than 36 years presented a stratifying effect on disease outcome. Our findings did not indicate major changes in trends of incidence of hypospadias. The years assessed did not have a significant effect on the number of cases.

Keywords Hypospadias, Congenital abnormalities, Birth defects, Developmental disabilities

1 Introduction

Hypospadias is a birth defect that occurs due to incomplete fusion of urethral folds during foetal development. It is marked by abnormal placement of the urethral opening, which occurs anywhere underneath the penis instead of the normal location at the tip of the glans affecting one in every 200–300 new born males [1].

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Causes appear to be multifactorial and may include hormonal factors, genetic changes as well as environmental influences. The urethra opening is un-orthotopically located and the penis is cosmetically different from the normal, which may importantly cause subfertility in adulthood due to poor projection of sperm and ejaculate fluid [2].

Hypospadias may occur as an isolated defect or in combination with other congenital anomalies such as undescended testis, scrotal bifid, vesical-ureteric refluxes, and inguinal hernias [3].

Importantly, Springer and associates [4] indicated that various research tools including PubMed, EMBASE and Google search engines demonstrated variations in occurrence, incidence, and global epidemiological trends of hypospadias. Although it is difficult to find definitive causes of hypospadias, this congenital abnormality may be a result of several factors, which may include endocrine factors, genetic influences as well as environmental circumstances [5].

Endocrine contributing factors may include an interruption in the synthesis bio-pathway of androgens, disrupting androgen receptors, or a sub-normal stimulation of testosterone hormone on human chorionic gonadotropin (hCG) [6].

Genetic abnormalities implicated in hypospadias include chromosomal abnormalities and malformed syndromes from anterior to penoscrotal forms, highlighting chromosome 46, XY disorders [5]. Kalfa et al. [7] reiterated that hypospadias malformation appeared to be at a crossroads of various mechanisms involving genetic and environmental factors. The genes of penile development (HOX, FGF, Shh), testicular determination (WT1, SRY) and those regulating the synthesis of the luteinizing hormone (LH) receptor, as well as the action of androgen (5alpha reductase, androgen receptor) may cause hypospadias when altered.

It is interesting to note that hypospadias abnormalities may also be of paternal inheritance [5]. The role of environmental factors might be associated with endocrine disruptors, among these are agents used in viticulture, which include vinclozolin, procymidone and linuron. In addition, nitrates are a group of inorganic pollutants implicated in disruption of gonadal steroidogenesis [8]. Agricultural-, and pesticide substances, pharmaceutical products as well as plant oestrogens are also possible causative agents of hypospadias [9].

Improved reporting systems may have caused the increase in prevalence of hypospadias since reporting of mild cases as well as decreased mortality rates of premature babies has improved, mainly due to improved antenatal and postnatal health care reporting services [10, 11]. Despite an increase in the prevalence of hypospadias, the definitive cause is not yet known. The prevalence of hypospadias was reported to have increased during the past thirty years, which may in part be associated with increased genetic modifications, environmental pollution, increased survival rates of low-birth-weight babies, as well as changes in reporting due to improved reporting instruments [2]. Genetic disorders, especially in familial and syndromic forms where hypospadias occurs due to abnormal genital development (phallus or testicular dysgenesis) or associated with a defect in the androgenic pathway represents 20% of cases, while the remaining 80% of cases occur idiopathically [7]. Most of the idiopathic causes are linked with intrauterine growth retardation (IUGR) and babies that are small for gestational age (SGA).

The diagnosis of hypospadias is usually at birth as one of the physically assessed congenital anomalies. A method designed to assess congenital abnormalities is the case–control model. The evaluation of the prevalence of hypospadias at birth is a challenge in that the number of fetuses with hypospadias that die through abortions, remain unknown and hence are not accounted for in the evaluation. However, the closest figures that may fairly indicate the actual prevalence of hypospadias is the prevalence at birth. Imaging tools such as ultrasonography (US) evaluation may be useful in detecting other abnormalities during pregnancy. However, such tools are not validated for evaluation of hypospadias [12]. Inadequacy of community awareness of hypospadias, especially in poor-resource settings with large numbers of children requiring surgery, is of a great concern since health facilities are often too far to obtain timely healthcare services and community members are often too poor to get adequate and comprehensive treatment [13]. A study conducted in the United States demonstrated disease burden for cryptorchidism and hypospadias as quantified by determination of utilization of health care facilities in comparison with the economic outcomes of the disease [14]. Furthermore, hypospadias disease burden was reflected by a Dutch study group which reported an increased prevalence of about 3.8/1000 male babies [15].

The burden of surgical congenital anomalies in Africa was further highlighted by a population-based study conducted across Kenya [16]. In view of congenital anomalies reported locally, social challenges caused by hypospadias were seen as crucial to not only repair and treat hypospadias defects, but also to conduct a study to determine trends and predictors of hypospadias, and contribute towards minimizing hypospadias incidence, especially if the risk factors can be avoided. Our study aimed at investigating the trends in incidence of hypospadias and its possible determinants among male babies born at a tertiary hospital during a 3-year period. Principle objectives

included determination of the annual incidence of hypospadias, trends in the incidence of hypospadias and the associated socio-economic and demographic characteristics of mothers of male babies born with and without hypospadias. Furthermore, to determine predisposing factor/s that may possibly be responsible for hypospadias.

2 Methods

2.1 Study setting and design

This study was conducted at Charlotte Maxeke Johannesburg Academic Hospital (CMJAH) at the transfer unit of the labour ward in the Department of Gynecology and Obstetrics. This hospital is one of the tertiary hospitals in South Africa situated in Johannesburg, a cosmopolitan city with major economic development. The study design was a retrospective case–control study using patients' medical records from 1 January 2014 to 31 December 2016.

2.2 Ethical consideration

Ethical approval was obtained for this study prior to data collection, from the University of the Witwatersrand Human Research Ethics Committee (HREC medical) with Clearance Certificate Number: M191143.

Permission had also been obtained directly from the Head of Department of Gynecology and Obstetrics as well as from the Chief Executive Officer (CEO) of CMJAH to accessed stored medical records. The study procedures were in accordance with the Declaration of Helsinki of 1964 and its more recent revision of 2013.

Data collected from patient mother's records, were de-identified to ensure study participant confidentiality.

2.3 Study population

The study included records of all mothers who delivered baby boys with hypospadias defects (cases) as well as mothers who delivered baby boys without hypospadias defects (controls), within the same period of less than 2 weeks apart in the ratio of 1:2, respectively. A total of 221 mothers file records matched our interest, of which 73 were hypospadias cases and 148 controls. Since hypospadias is regarded as a rare occurrence with few cases, the controls (new born boys without hypospadias) numbers, were doubled in order to increase power and efficiency so as to achieve accurate statistical analyses.

2.4 Variables

The outcome variables were the presence or absence of hypospadias whilst independent variables assessed included delivery year, mother's marital status, mother's medical history, mother's surgical history, mother's antenatal vaccination, mother's age, mode of delivery, baby's gestational age in weeks, mother's family history relevant to chronic medical pathologies, mother's congenital abnormalities, mother's life style such as smoking history, alcohol use, use of traditional herbal medicine, mother's employment status, mother's level of education, single or multiple pregnancies and baby's birth weight in grams.

2.5 Inclusion criteria

"Inclusion criteria: All mothers registered in the Department of Gynecology and Obstetrics at CMJAH, delivery registries, folders and files during the specified study time period of three years (January 12014–December 31 2016) who gave birth to live baby boys.

The case sample collection criteria were: mothers of all baby boys diagnosed with hypospadias at birth, born within a period of 2 weeks (maximum) from the birth of corresponding controls without hypospadias.

The control sample selection criteria were: mothers of baby boys without any physical abnormalities including hypospadias, cryptorchidism, Down syndrome or cleft lip/palate born within a period of 2 weeks (maximum) from the birth of a corresponding case with hypospadias.

2.6 Data collection

Data were collected retrospectively from patient mother's records. Mothers' hospital registers were used to search and identify cases and controls. Mothers' hospital files for baby boys born with and baby boys born without hypospadias who were born within-two weeks' time apart were retrieved.

The keywords used in the search were hypospadias, birth defects, congenital abnormality, and developmental disabilities. Only data files of babies born with hypospadias and babies born without hypospadias within the same period, same day or at least less than 2 weeks apart, were selected and considered for the study.

The baby's diagnosis and time of birth were found hand-written on the consent form signed by the attending doctor while the mother's demographic information was printed on the first page of the admission file. Information regarding the mother's medical, surgical, and gynecological/obstetrics history including both pre and perinatal information and the newly born baby's physical and medical information were identified in the mother's files. All variables were assessed according to the data collection form. The data were collected using self-designed data-collection forms. Data were entered into EpiData 3.1, an electronic data base, and subsequently the data were exported into STATA version 15.1 for the cleaning, coding, and data analysis processes.

2.7 Data analysis and statistical methods

The categorical variables were summarized using frequencies and percentages. Hypotheses for difference in

frequencies were tested using the Pearson Chi-squared test or the Fisher's exact test as applicable for the crude odds ratios (OR), while using the Mantel Haenszel (M-H) method and the Woolf method to construct the 95% confidence intervals of odds ratios. Unadjusted/simple and adjusted/multiple logistic regression procedures were used to determine the association between the response variable, hypospadias outcome, and the predictor variables. Unadjusted and adjusted odds ratios with corresponding 95% CIs were reported. A p value of less than 0.05 was considered statistically significant.

3 Results

Table 1 presents frequencies (percentages) from 2014 to 2016, with the frequencies (percentages) per mother's socio-demographic characteristics and the baby birth weights, indicated in cases and controls.

Table 1 indicates that the change in percentage of hypospadias cases and controls are statistically equal throughout these three years ($p=0.99$). Therefore, the year variable had no significant effect on the number of hypospadias cases.

Similarly, marital status ($p=0.38$), medical history ($p=0.22$), surgical history ($p=0.50$), vaccination ($p=0.86$), family medical history ($p=0.33$), smoking history ($p=0.40$), employment status ($p=0.65$) and number of pregnancies ($p=0.28$) had no significant effect on hypospadias outcome. The variables: mother's age ($p=0.07$), mother's congenital abnormalities ($p=0.06$) and mother's education ($p=0.08$) showed no statistically significant effect in this study, however, it has a medically significant effect on boys' hypospadias. Importantly, baby boys born by Caesarian Section (CS) ($p<0.001$), and baby boys with a low gestational age ($p=0.002$) are more likely to have hypospadias, compared with those born by spontaneous vaginal delivery (SVD) and with normal gestational age.

This table shows the association between hypospadias and potential risk factors related to maternal medical and surgical history, the mother's economic status and the baby boys' physical status at birth.

Table 1 Association between hypospadias and potential risk factors

Variable	Annual trend	Cases ($n=73$) (%)	Controls ($n=148$) (%)	p value
Year	2014	17 (23.3)	35 (23.7)	0.99
	2015	32 (43.8)	67 (45.3)	
	2016	24 (32.9)	46 (31.1)	
Marital status	Single	20 (27.4)	35 (36.5)	0.38
	Married	47 (64.4)	85 (57.4)	
	Others	6 (8.2)	9 (6.1)	
Medical history	Yes	4 (5.5)	3 (2.0)	0.22*
Surgical history	Yes	14 (19.)	23 (15.5)	0.50
Vaccination history	Yes	64 (87.7)	131 (88.5)	0.86
Mother's age	Median (IQR)	35 (30–40)	37 (33–40)	0.07
Caesarian section	Yes	19 (26.0)	12 (8.1)	**< 0.001**
Baby's' gestational age	Median (IQR)	38 (32–39)	38 (36–40)	**0.002**
Familial medical history	Yes	1 (1.4)	0 (0)	0.33
Congenital abnormalities	No	66 (90.4)	143 (96.6)	0.06+
Smoking history	Yes	3 (4.1)	3 (2.0)	0.40
Alcohol use	Yes	10 (13.9)	3 (2.1)	**0.001***
Drug use	Yes	23 (31.5)	1 (0.7)	**< 0.001**
	Unknown	5 (6.9)	13 (8.8)	
Traditional herbal use	Yes	17 (23.3)	15 (10.1	**0.03**
	Unknown	10 (13.7)	18 (12.2)	
Employment	Employed	43 (58.9)	93 (62.8)	0.65+
	Unemployed	2 (2.7)	2 (1.4)	
Education	At least high school	60 (82.2)	134 (95.5)	0.08
Multiple pregnancies	More than one baby	8 (11.0)	10 (6.8)	0.28
Baby birth weight (g)	Median (IQR)	2490 (1700–3190)	3195 (2430–3755)	**< 0.001**

*Used Fisher's exact, + all answers were No or Unknown. The denominator is 147 (1 unknown control) one case and 5 controls excluded – answers unknown), p values in bold are statistically significant

Boys born from mothers who use alcohol ($p=0.001$), drugs ($p<0.0001$) and traditional herbal medicine ($p=0.03$) were more likely to be born with hypospadias than boys born from mothers who did not use these substances.

Babies born with a low birth weight (< 2500 g) were more likely to be born with hypospadias compared with those born with a birth weight of more than 2500 g.

Table 2 shows the association between hypospadias outcome, and stratified mother's age in relation to possible predicting factors such as the mother's lifestyle, medical history, sociodemographic characteristics as well as the baby's birth weight and gestational age stratified by the mother's age group (< 36 years or ≥ 36 years). The results for crude odds ratios, without taking stratification into account, are similar to those reported in Table 1. Therefore, the same conclusions may be drawn as shown by the forest plot in Fig. 1.

When stratification is considered, crude odds ratios become meaningless. Therefore, instead, the combined M-H odds ratios were used in order for the results to become meaningful.

The variables: mother's mode of delivery, mother's history of alcohol consumption, and mother's traditional herbal use are significant risk factors in baby boys' hypospadias. The respective combined M-H odds ratios of 3.93, 2.87, 1.95 are larger than one and their 95% confidence intervals of (1.81; 8.55), (1.11; 7.41) and (1.05; 3.63) do not include one. The analysis of maternal age above 36 years presented an effect on stratification with the likelihood of hypospadias occurrence. Furthermore, baby boys born with normal weights (≥ 2500 g) were less likely to be born with hypospadias (M-H OR (95% CI) = 0.35 (0.19; 0.62)). It is clear that normal birth weight is protective against hypospadias since the M-H OR 0.35 < 1 and the 95% confidence interval (0.19; 0.62) does not include one. These results may also be observed in the forest plot as shown in Fig. 2.

Table 3 presents the odds ratios and the associated 95% confidence intervals obtained by fitting the unadjusted and the adjusted logistic regressions to data where the positive response was the case, and the predictor variables were more or less the same as the ones presented in the previous two tables (Tables 1, 2).

Simple logistic regression indicated that baby gestational age is significantly associated with hypospadias outcome, whereas a later gestational age is protective ((OR 0.38; 95% CI (0.21; 0.71)). This also is true for baby birth weights where the odds ratio and its 95% confidence limits were less than one when comparing baby boys born with normal weights with those born with low birth weights.

Alcohol use (OR 3.10; 95% CI (1.19; 8.09)) and traditional herbal use ((OR 2.04; 95% CI (1.11; 3.78)) were significantly associated with the occurrence of hypospadias in new- born babies.

When the adjusted logistic regression model was fitted to the data, that is when all the predictor variables were mutually considered, only the mode of delivery and the baby's birth weights have a significant influence on the occurrence of hypospadias (OR 3.73; 95% CI (1.50;9.27) and (OR 0.32; 95% CI 0.17;0.63), respectively. This was not the case when the unadjusted

Table 2 Association between hypospadias and stratified maternal age

Variables	Crude analysis OR (95% CI)	Stratified age Analysis OR (95% CI)		Combined M-H OR (95% CI)
		< 36 years	≥ 36 years	
Mothers' previous medical history	2.80 (0.61; 12.86)	2.59 (0.41; 16.15)	2.62 (0.16; 43.30)	2.60 (0.56; 12.05)
Mothers' previous surgical history	1.29 (0.62; 2.68)	0.87 (0.32; 2.38)	2.04 (0.69; 5.98)	1.27 (0.61; 2.64)
Mothers' prenatal vaccination	0.92 (0.39; 2.18)	1.24 (0.35; 4.39)	0.66 (0.20; 2.16)	0.89 (0.38; 2.13)
Mothers' mode of delivery	3.99 (1.81; 8.77)	1.78 (0.58; 5.47)	9.6 (2.99; 30.75)	3.93 (1.81; 8.55)
Mothers' history of congenital abnormalities	3.03 (0.93; 9.91)	2.98 (0.67; 13.17)	2.68 (3.59; 19.94)	2.88 (0.87; 9.49)
Mothers' smoking history	1.54 (0.34; 7.08)	0.82 (0.72; 9.34)	2.68 (0.56; 19.94)	1.59 (0.35; 7.22)
Mothers' history of alcohol consumption	3.10 (1.19; 8.09)	1.76 (0.53; 5.84)	7.5 (1.37; 41.10)	2.87 (1.11; 7.41)
Traditional herbal use by Mothers	2.05 (1.11; 3.78)	1.94 (0,88; 4.39)	1.93 (0.73; 5.09)	1.95 (1.05; 3.63)
Mothers' employment status	0.85 (0.48; 1.50)	1.49 (0.66; 3.39)	0.40 (0.17; 0.96)	0.81 (0.45; 1.43)
Mothers' educational level (high education is taken as reference)	0.48 (0,21; 1.09)	0.80 (0.29:2.18)	0.20 (0.45; 0.91)	0.53 (0.24; 1.19)
Number of babies born at a time by mother	1.69 (0.64; 4.50)	1.74 (0.47; 6.39)	1.6 (0.36; 7.16)	1.68 (0.63; 4.48)
Babies' birth weight	0.35 (0.19; 0.63)	0.32 (1.45; 0.72)	0.38 (0.16; 0.89)	0.35 (0.19; 0.62)

Stratified maternal age, Crude OR, Mantel Haenszel combined, analysis by the Woolf approach

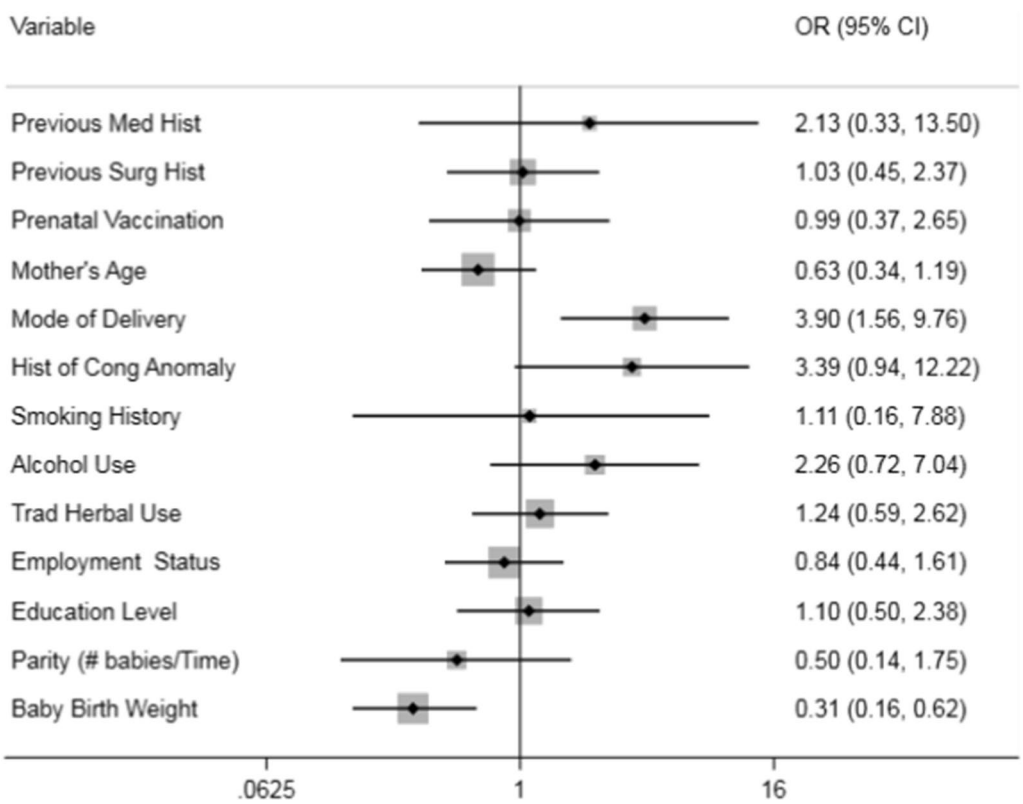

Fig. 1 Forest plot of crude odds ratios

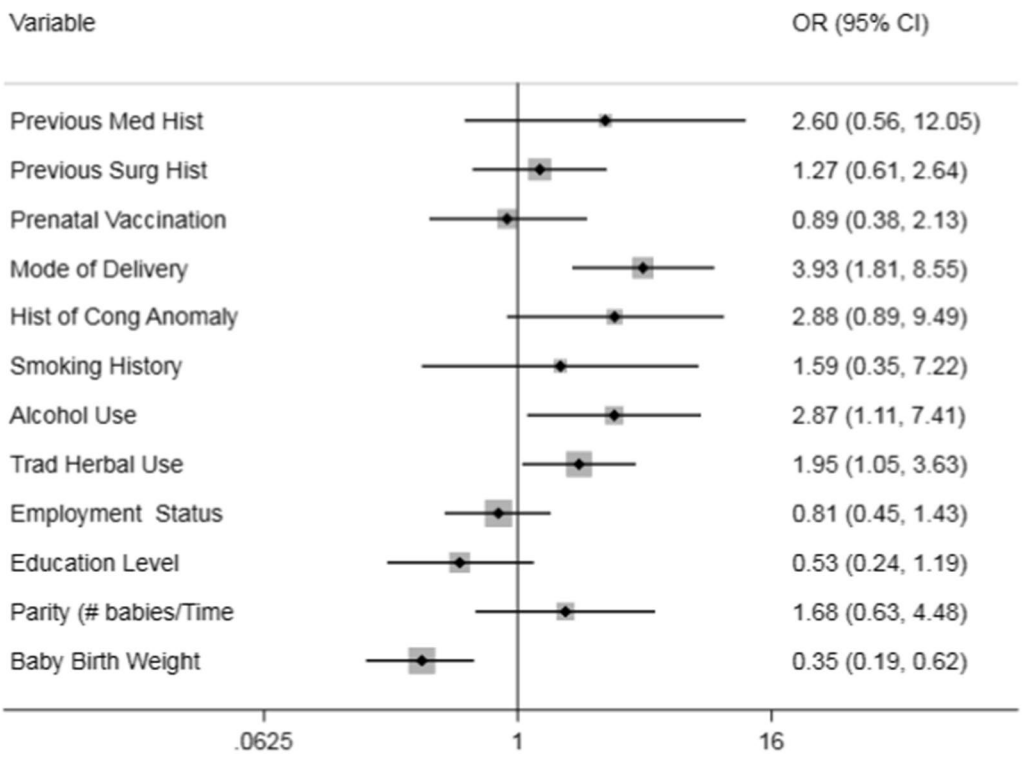

Fig. 2 Forest plot for combined Mantel Haenszel odds ratios

Table 3 Unadjusted/simple and adjusted/multiple logistic regression of variables

Variables	Unadjusted/simple logistic regression OR (95% CI)	Adjusted/multiple logistic regression OR (95% CI)
Mothers' previous medical History	2.80 (0.61; 12.86)	2.30 (0.37; 14.24)
Mothers' previous surgical History	1.28 (0.62; 2.68)	1.05 (0.46; 2.40)
Mothers' known acquired abnormalities	1.54 (0.34; 7.08)	2.13 (0.71; 6.41)
Smoking history	2.07 (0.41; 10.53)	1.08 (0.15; 7.62)
Baby's gestational age	0.38 (0.21; 0.71)	0.94 (0.86; 1.09)
Mothers' congenital abnormalities	3.03 (0.93; 9.91)	3.52 (0.99; 12.58)
Alcohol use	3.10 (1.19; 8.09)	2.33 (0.74; 7.28)
Traditional herbal medicine	2.04 (1.11; 3.78)	0.30 (0.62; 2.74)
Employment status	0.85 (0.48; 1.50)	0.89 (0.47; 1.70)
Level of education	0.48 (0.21; 1.18)	1.13 (0.52; 2.43)
Multiple pregnancy	1.69 (0.64; 4.50)	0.50 (0.14; 1.72)
Baby's birth weight	0.34 (0.19; 0.63)	0.32 (0.17; 0.63)

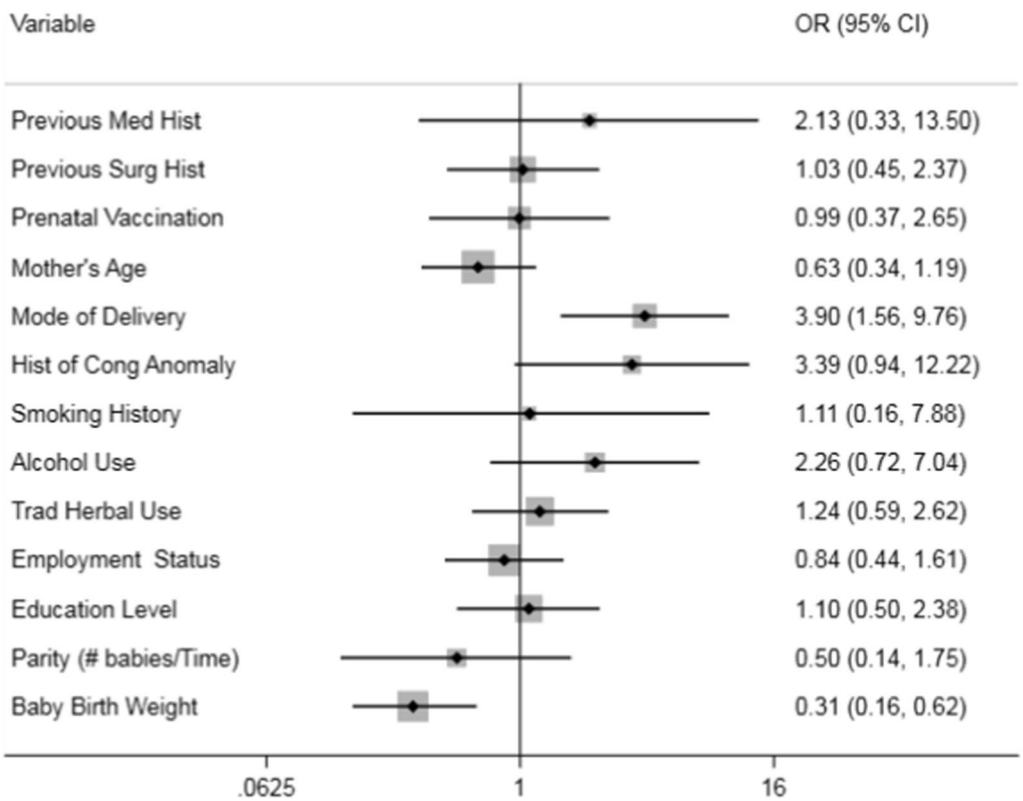

Fig. 3 Forest plot of odds ratios using multiple logistic regression

logistic regression was fitted to the data. These results are confirmed by the forest plot shown in Fig. 3.

4 Discussion

The important outcomes of this case–control study on the assessment of potentially predicting factors associated with hypospadias including mode of delivery, maternal advanced age, alcohol use, traditional herbal use, and low birth weight, are that all the mentioned factors independently increase the likelihood of an infant being born with hypospadias.

The most important association revealed in this study is the increased risk of hypospadias amongst boys born by CS as one of the supportive modes of delivery, combined M-H (OR 3.93; 95% CI 1.81; 5.55). According to Sides and co-workers, six fetuses who were prospectively and sonographically suspected to have hypospadias, especially in combination with other abnormalities, were born by aided procedures such as induction, vacuum assisted or and CS [17]. Having carried out this study at a referral and tertiary facility with available obstetric resources, provided an opportunity of finding an association between hypospadias and assisted mode of deliveries.

The odds ratio for mode of delivery of boys with hypospadias was by far the strongest effect observed in our study, with an OR 3.93 (95% CI 1.81; 8.55).

In an analysis of joined exposure to smoking and alcohol consumption, maternal smoking was associated with a reduced risk of hypospadias M-H OR 1.59 (95% CI 0.35; 7.22) with an unremarkable age stratification effect. The interpretation of our findings on the smoking variable does not suggest that this exposure has an overall benefit to a pregnant woman or to an unborn baby, it may however, point to understanding mechanisms that lead to hypospadias [18].

Our findings for the smoking variable concur with a meta-analysis [19] reported that maternal smoking may be associated with a modest decreased risk of hypospadias. We speculate that maternal smoking may influence the risk of developing hypospadias by means of its endocrine effects. Smoking is associated with maternal oestrogen reduction and related inhibition of placental aromatase, It is well documented that aromatase converts testosterone to estradiol [19]. The age-related stratification with augmentation risk for hypospadias was highlighted in our study. This concurs with a study conducted in China assessing characteristics of the mothers' pregnancies. It was reported that hypospadias was more likely to occur in infants born by relatively aged mothers above thirty-five years. In the same study, advanced maternal age was found to be associated with an increased incidence of structural birth defects including urethral abnormalities [20]. Likewise, we identified a significant relationship between hypospadias and advanced maternal age. Our study further indicated an association between maternal alcohol consumption and the risk of developing hypospadias using unadjusted logistic regression OR 3.10; (95% CI 1.19; 8.09). Similar findings were reported by Xu et al. [20], who emphasized that unlike previous studies, their findings suggested that maternal alcohol consumption during the perinatal period may be associated with hypospadias. Other risk factors identified to be associated with hypospadias include maternal traditional herbal use. However, relatively little is known about the types of herbal medicines used by the mothers.

There were a few limitations to our study. Firstly, the study was conducted retrospectively, which limited real-time data capture and evaluation. Secondly, the study was a case–control study and not a cohort, limiting to the follow-up of subjects, which may possibly cause figurative and numerical errors and even omissions. We reiterate the fact that not all potential parental, foetal and environmental risk factors were included in the analysis, these would be unaccounted co-founding factors such as paternal factors. Hence, further prospective research through multiple approaches to a greater extent is necessary. Thirdly, only a three-year study was conducted at a single centre tertiary facility, which may have resulted inaccurate account of our study results, hence larger scale studies across all levels of health care facilities including primary health facilities, public- and private hospitals without forgetting mothers who deliver from home are recommended. Nevertheless, this study was conducted because community awareness of hypospadias outcome and preventive measures for possible exposures are important to minimize the incidence of hypospadias and contribute to knowledge on a disease which is scarcely studied in our country.

5 Conclusions

Maternal age above 36 years appeared to have a stratification effect on hypospadias presentation. The trends in incidence of clinically diagnosed hypospadias at birth did not indicate major changes over time. The years assessed did not have a significant effect on the number of cases. The study findings sought to bring awareness of hypospadias to facilitate the management and to prevent possible predicting factors in a triad of community awareness, early detection, and prompt surgical management to minimize outcome.

Abbreviations

CDC	Centres for Disease Control and Prevention
CDS	Colour Doppler Sonography
CI	Confidence interval

CMJAH	Charlotte Maxeke Johannesburg Academic Hospital
CS	Caesarian Section
DSD	Disorders of sexual development
g	Grams
hCG	Human chorionic gonadotropin
IQR	Inter quartile range
IUGR	Intrauterine growth retardation
LH	Luteinizing hormone
OR	Odds ratio
SD	Standard deviation
SGA	Small for gestational age
Shh	Sonic hedgehog
SRY	Sex-determining Region Y protein
SVD	Spontaneous vaginal delivery
TU	Transfer unit
M-H	Mantel Haenszel
UNISA	University of South Africa
US	Ultra sonography
WITS	University of the Witwatersrand

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Author contributions
UD: Conception of ideas, literature review, protocol development, data collection, data analysis, manuscript preparation and corresponding author. AA: Supervision of protocol development, scientific and technical reviews. KG: Entire review of research study, data management, data analysis and interpretation, proof-reading and re-editing. NM: Supervision of protocol development, proof-reading and re-editing, re-alignment of tables and graphics. All authors read and approved the final manuscript.

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Availability of data and materials
The datasets used and analysed during this study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
The Human Research Ethics Committee (Medical) of the University of the Witwatersrand approved this study (Reference number: M 191143).

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

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