

# Prevalence and Associated Risk Factors of Preputial and Penile Abnormalities Among Voluntary Medical Male Circumcision Clients in KwaZulu-Natal Province, South Africa

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## Research Article

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# Abstract

## Background

Voluntary Medical male circumcision (VMMC) has been identified as a cost-effective intervention for reducing the transmission of HIV. KwaZulu-Natal (KZN), the second most populous province in South Africa, has the highest HIV prevalence, estimated at 27%. VMMC reduces the transmission of HIV by up to 60%; at initiation of VMMC Program in 2010, the KZN VMMC target was 2.4 million, almost 50% of the national target, among males aged 15-49 years. This paper documents the prevalence of penile abnormalities and related factors among clients undergoing VMMC procedures in KwaZulu-Natal province.

## Methods

A retrospective review of files was conducted among VMMC clients at the Centre of Excellence (a referral centre in the KZN province) and data was captured from a standardized client form into an Excel database. The data was analysed using STATA 15.0. Univariate and multivariate analysis were done using Logistic regression was used to determine factors associated with penile abnormalities.

## Results

During the review period, 6,650 males accessed VMMC services; the median age was 13 years (IQR 9 – 21). A total of 227 (3.4%) of the clients were HIV-Positive, about 80% of these aged  $\geq 13$  years. Upon physical examination, 5,366 (80.6%) of the VMMC clients had penile abnormalities (Mild 781, Moderate 2,282, Severe 2,303). Overall, 43% of these clients had severe penile abnormalities (SPA); two-thirds were aged below 13 years and 10% aged above 34 years. The three most common Penile Abnormalities (PA) were phimosis (3,686; 55.4%), tight ring (3,669; 55.2%) and overhanging foreskin (2,966; 44.6%). The odds of penile abnormality were significantly lower in older clients aged 13–18 years (AOR = 0.74; 95% CI = 0.59–0.87) and above 18 years (AOR = 0.15; 95% CI = 0.10–0.29) compared to younger clients aged below 13 years.

## Conclusions

A higher prevalence of Penile Abnormalities was observed among the younger clients except for balanitis / posthitis. Recommendations for VMMC program include the fact that all clients need to be examined thoroughly preoperatively to exclude any abnormalities. Any clients with severe abnormalities should be referred for specialist examination and surgery.

## Background

Human immunodeficiency virus (HIV) ranks as a top global cause of morbidity and mortality. Since the identification of the HIV epidemic, over 70 million individuals have acquired the virus, of whom 50% have

died. At the end of 2018, global prevalence estimates suggest that 37.9 [32.7–44.0] million people were living with HIV with some geographical regions being more affected than others (1).

Sub-Saharan Africa still carries a disproportionate burden of HIV with an estimated one in every 25 adults (4.4%) living with HIV. This accounts for approximately 70% of global HIV infections. Out of the estimated 6,000 new infections that occur worldwide each day, two thirds occur in sub-Saharan Africa. As such, successful interventions for HIV prevention in this region could have a major impact on the overall burden of HIV worldwide (1).

According to 2019 UNAIDS estimates, South Africa has an overall HIV prevalence rate of 20,4% (7,7 million people living with HIV) (2). KwaZulu-Natal Province harbours an overall HIV prevalence of 27%, the highest among the nine provinces that constitutes the geopolitical structure of South Africans' landscape (3). In this province, 12% of youth in the age category 15–24 years live with HIV infection, the highest compared to the other provinces (4). Interventions such as antiretroviral treatment (ART) have been widely rolled out due to their beneficial effect of improving the quality of life and reducing transmission and mortality (5). However, to achieve an AIDS free generation, there is need to enhance combination intervention strategies and expand access to VMMC (6, 7) as an additional preventive strategy targeted at reducing HIV acquisition among men.

Findings from randomised controlled trials done in three sub-Saharan African countries as well as data from mathematical modelling reaffirmed the evidence in support of the efficacy of VMMC for preventing men's risk of heterosexual acquisition of HIV. This evidence reinforced WHO (8) to make the recommendation for a large scale roll-out of VMMC as an essential component of HIV preventive strategy that could effectively help reduce heterosexually acquired HIV (9–14). Further, a meta-analysis including 49 studies revealed that VMMC was protective against HIV infection for both homosexual and heterosexual men (15). With an 80% coverage of VMMC among HIV negative men in the countries with high prevalence of HIV and low VMMC uptake would provide a substantial threshold for sustained prevention of HIV transmission at population level. Since the prevention strategy was established in 2007, over 18 million men have been medically circumcised in sub Saharan Africa countries to date. Of these close to 5 million procedures were done in South Africa (16). VMMC uptake in these countries has ranged from 10–63% (16). This provides some light as to the acceptability of this strategy in countries where circumcision is not the traditional norm. VMMC has the potential to alter current HIV epidemic trajectory in sub Saharan Africa if effectively combined with other proven intervention mentioned earlier (17, 18).

From a public health perspective, strategies to optimize expansion of existing proven interventions as well as creating demand for uptake of such existing interventions within resource limited areas need to be enhanced (19, 20). In view of this there is need to reinforce improvement of the surgical procedures through use of novel surgical approaches so as to deliver safe and high quality VMMC services which minimise post-surgical complications and maximize public health benefits (8, 21). The PrePex<sup>®</sup> and ShangRing<sup>®</sup> foreskin crushing devices were approved by the WHO after a series of evidence generated from clinical trials conducted among adult males in 5 countries in sub Saharan Africa (22–24). However,

the trials conducted on PrePex<sup>®</sup> and ShangRing<sup>®</sup> systematically excluded males with preputial / penile and preputial / penile scrotal abnormalities and diseases. These include phimosis, paraphimosis, warts or ulcers of the prepuce, active genital infection, hypospadias, torn or tight frenulum including anatomical abnormalities and any other preputial / penile pathological conditions that the opinion of the investigator would impede device placement for a thorough VMMC procedure. Evaluating the performance PrePex<sup>®</sup> and ShangRing<sup>®</sup> devices by the WHO technical committee found that among the study participants 7% among PrePex<sup>®</sup> and 1% of ShangRing<sup>®</sup> were not eligible for circumcision (22, 25). It is therefore essential to understand the burden of preputial / penile abnormalities identified pre-surgically as this has an impact on effective expansion of VMMC program but also need to be taken into account so that new devices that could be able to accommodate common abnormalities could be made available in the market for use. This study was therefore carried out to assess the prevalence and related factors of preoperative preputial / penile abnormalities during the VMMC among young and adult males in KwaZulu-Natal Province.

## Methods

This study was a retrospective record review of participant records presenting for VMMC at the Northdale Hospital, Medical Male Circumcision Center of Excellence, in KwaZulu-Natal Province, South Africa between January 2012 and July 2016. There were 6,650 participants ranging from less than 8 years to greater than 35 years old. All participants or their legal guardians consented to VMMC and HIV testing prior to the procedure. Inclusion into the study considered men who presented for VMMC at the clinic during the time period that the study was done and de-identified data were extracted from the client database. Prior to analysis, data were interrogated and assessed for errors and completeness. Data were cleaned and all errors identified were appropriately corrected. Data obtained included demographics, recorded penile abnormalities and HIV test results. Age data included those below 8 years, 8–12, 13–18, 19–34, and  $\geq 35$  years old. Consent to do an HIV test was obtained prior to the test, and appropriate consent obtained prior to the circumcision procedure. Prior to analysis, data were de-identified to maintain anonymity of the participants and protect their confidentiality. Data were analysed using Stata version 13.0 (StataCorp Limited, College Station, Texas, USA). Univariate analysis was performed to describe the frequency distribution of the characteristics of the study participants as well as their relationship to identification of preputial / penile abnormalities. Multivariate regression analysis was done to evaluate independent factors associated with identifiable preputial / penile abnormalities. Two-sided p values of  $< 0.05$  were considered statistically significant.

## Results

### Characteristics of participants with preputial / penile abnormalities presenting for VMMC

There were 6,650 males who attended the VMMC program during the period under review. The participants had a median age distribution of 13.2 years (IQR 9.1–21.7 years) (Table 1). The VMMC program was mostly carried out in a public hospital (n = 5,176; 77.8%). A greater proportion of men undertaking circumcision procedure in this study were tested for HIV infection of which 82.4% (n = 5,480) of them were HIV negative. Over half of the study participants came for VMMC services either for partial HIV reduction (n = 3,491; 52.4%) or for hygiene reasons (n = 3,455; 51.9%). Approximately, one out of five participants accessed VMMC services for religious reasons or sexual pleasure.

Table 1  
 Characteristics of participants who presented for VMMC procedure in KwaZulu Natal Province by age group

Variable	Total	Under 8	8–12	13–18	18–34	>35
N	6650	1411 (21.2%)	1950 (29.3%)	1425 (21.4%)	1313 (19.7%)	551 (8.3%)
Median age, years (IQR)	13.2(9.1–21.7)	3.9(1.8–5.9)	11.2(9.7–12.1)	15.0(13.8–16.6)	22.0(22.0–29.7)	45.2(39.1–65.5)
Type of MMC Site						
Public Hospital	5176 (77.8%)	1093 (21.1%)	1462 (28.2%)	1171 (22.6%)	1045 (20.2%)	404 (7.8%)
Outreach site	677 (10.2%)	163 (24.0%)	196 (28.9%)	115 (16.9%)	136 (20.1%)	67 (9.9%)
Other*	797 (12.0%)	155 (19.4%)	292 (36.6%)	139 (17.4%)	60 (7.5%)	79 (9.9%)
Indication for VMMC						
HIV reduction	3491 (52.4%)	597 (17.1%)	1102 (31.6%)	866 (24.8%)	666 (19.0%)	260 (7.4%)
Hygiene	3455 (51.9%)	792 (22.9%)	1002 (29.0%)	624 (18.1%)	744 (21.5%)	293 (8.5%)
STI reduction	2939 (44.2%)	517 (17.6%)	874 (29.7%)	689 (23.4%)	630 (21.4%)	229 (7.8%)
Sexual pleasure	1087 (16.3%)	229 (21.1%)	301 (27.6%)	219 (20.1%)	243 (22.3%)	95 (8.7%)
Religious / social	421 (6.3%)	187 (44.4%)	78 (18.5%)	53 (12.6%)	61 (14.4%)	42 (9.9%)
HIV test result						
Negative	5480 (82.4%)	1134 (20.7%)	1574 (28.7%)	1244 (22.7%)	1088 (19.8%)	440 (8.0%)
Positive	227 (3.4%)	11(4.8%)	20 (8.8%)	30 (13.2%)	100 (44.1%)	66 (29.1%)
Unknown	186 (2.8%)	51 (27.4%)	84 (45.2%)	30 (16.1%)	19 (10.2%)	2 (1.1%)
Missing	757 (11.4%)	215 (28.4%)	272 (35.9%)	121(15.9%)	106 (14.0%)	43 (5.7%)
*Other includes Mass event, Mission or Private Hospital						

The overall prevalence of preputial / penile abnormalities was 80.6% (n = 5,366) (Table 2). There were considerable variations in occurrence by age with adults over 35 years (n = 456; 8.5%), children under 8 years (n = 1,253; 23.3%) and 8–12 years (n = 1,581; 29.5%) having a greater proportion of penile abnormalities identified (Fig. 1). The most common abnormality identified was phimosis, which was highest in children aged 8–12 years (n = 1157; 31.3%), followed by children under 8 years (n = 1003; 27.2%) and lowest in adults age  $\geq$  35 (n = 288; 7.8%). A similar trend was demonstrated through a linear pattern of the occurrence of penile abnormalities being higher in the younger age group and lower in the older age group of the study population (Fig. 2). The exception to this was balanitis/posthitis which was more prevalent among the clients aged 19–34 years (n = 627; 46%) and lowest among the males aged 8–12 years (n = 131; 9.6%). Other abnormalities included tight ring, overhanging foreskin, adhesions between prepuce and glans, short frenulum and penile sores.

Table 2

Distribution of penile abnormalities among participants presenting for VMMC procedure by age category

Variable	Total N = 6650	Under 8 n/N (%)	8–12 n/N (%)	13–18 n/N (%)	19–34 n/N (%)	> 35 n/N (%)
Overall	5,366 (80.6%)	1,253 (23.3%)	1,581 (29.5%)	992 (18.5%)	1,084 (20.2%)	456 (8.5%)
Phimosis	3,686 (55.4%)	1003 (27.2%)	1157 (31.3%)	613 (16.6%)	625 (16.9%)	288 (7.8%)
Tight ring	3,669 (55.2%)	923 (25.1%)	1144 (31.1%)	703 (19.2%)	615 (16.8%)	284 (7.7%)
Overhanging foreskin	2,966 (44.6%)	886 (29.9%)	963 (32.4%)	375 (12.6%)	490 (16.5%)	252 (8.5%)
Adhesions	2,230 (33.5%)	918 (41.2%)	664 (29.8%)	228 (10.2%)	242 (10.8%)	178 (7.9%)
Balanitis/Posthitis	1,362 (20.5%)	175 (12.8%)	131 (9.6%)	250 (18.4%)	627 (46.0%)	179 (13.1%)
Short frenulum	1,136 (17.1%)	222 (19.5%)	393 (34.6%)	219 (19.3%)	207 (18.2%)	95 (8.4%)
Others	1,043 (15.7%)	341 (32.7%)	213 (20.4%)	143 (13.7%)	246 (23.6%)	100 (9.6%)

\*Others includes pearly penile papules & preputial/penile/perifrenular sores

## Factors associated with preputial / penile abnormalities among VMMC participants

In the univariate regression analysis knowledge of HIV status was significantly associated with preputial / penile abnormalities (Table 3). Participants who did not know their HIV status were significantly more

likely to be associated with preputial / penile abnormalities (UOR = 1.84; 95% CI 1.02–2.67) than those who knew their status. HIV positivity was significantly less likely to be associated with preputial / penile abnormalities (UOR = 0.29; 95% CI 0.05–0.63) compared to HIV negative status. Age category was significantly associated with penile abnormalities. Multivariate regression analysis revealed that with advancing age category, penile abnormalities were inversely associated with age, such that as age category increased, the association with penile abnormalities decreased (Table 3). Participants aged 13–18 (AOR 0.74; 95% CI 0.59–0.87) and > 18 years (AOR 0.15; 95% CI 0.10–0.29) were less likely to have penile abnormalities compared with male participants aged under 13 years of age.

Table 3  
Factors associated with penile abnormalities in KwaZulu Natal

Variable	Univariate UOR (CI)	p-value	Multivariate AOR(CI)	p-value
Age (years)				
< 13	1		1	
13–18	0.73(0.59–0.87)	< 0.001	0.74(0.59–0.87)	< 0.001
> 18	0.14(0.05–0.28)	0.044	0.15(0.10–0.29)	0.042
HIV test result				
Negative	1		1	
Positive	0.29(0.04–0.63)	0.089	0.27(0.08–0.62)	0.116
Unknown	1.84(1.02–2.67)	< 0.0001	1.80(1.01–2.62)	< 0.001
UOR – unadjusted odds ratios; AOR – adjusted odds ratios.				

## Discussion

The study showed that a higher proportion (82.4%) of men undergoing VMMC tested HIV negative. In this cohort, preputial / penile abnormalities were identified in 80.6%, with the most common abnormality being tight ring (n = 3,669) and phimosis (n = 3,686). The occurrence of preputial / penile abnormalities was highest among the clients aged below 13 years and lowest among the oldest age group of  $\geq 35$  years old. This pattern is consistent with previous findings where the prevalence of penile abnormalities was highest among the younger ages. These studies noted a trend where preputial / penile abnormalities declined as age increased (26, 27). Other preputial / penile abnormalities included such as preputial / penile sores, adhesions between prepuce and glands, balanitis/posthitis are similar to what has been reported in similar studies done in Johannesburg and Swaziland (26, 27).

The study indicates that half of the clients accessed VMMC services for partial reduction risk of acquiring HIV infection. Knowledge of HIV status was significantly associated with penile abnormalities such that

participants who did not know their HIV status were significantly more likely to be associated with penile abnormalities (AOR = 1.80; 95% CI 1.01–2.62). This might be partly due to the fact that individuals who were more conscious about their HIV status might have had further consultations prior to attending the VMMC program. It is also plausible that since the prevalence of preputial / penile abnormalities was highest among the clients aged below 13 years who may not have sufficient knowledge regarding their own HIV infection, that factor may have driven this observed relationship. We don't seem to think of any physiologically plausible explanation as to the nature of this relationship other than understanding the effect of age and exposure to HIV information of youth. Despite our understanding, we still seem to suggest that this finding needs to be further interrogated possibly with larger sample to validate the relationship between preputial / penile abnormalities and knowledge of HIV transmission. A previous study done by Mukudu et al., had a similar observation (26).

The effect of age on penile abnormalities was also shown in a multivariate regression analysis (28). We found that an increase in age category was inversely associated with penile abnormalities. There was observed linear relation whereas age category increased and there was a corresponding decline in the strength of the association with penile abnormalities. Those who were aged 13–18 had 0.74 times the odds of penile abnormalities while those who were > 18 years had 0.15 times the odds of penile abnormalities compared with male's participants aged under 13 years. These findings are consistent with the results of Mukudu et al., in their Soweto study where the higher odds of penile abnormalities associated with decreasing age of VMMC clients (26).

A significant risk of genital malformations was associated with maternal and/or paternal occupational exposure to endocrine-disrupting chemicals (EDCs) across a number of studies (29–31). One case-control study in France found clear evidence of a relationship between parental occupational/environmental exposure to pesticides (OR 4.41) and male genital malformations in offspring (31). This was partly explained by the difference in impact that each EDC has on each androgen-dependent male genital abnormality or by the timing of fetal exposure. However, although prenatal contamination by EDCs maybe a risk factor for newborn male external genital malformations, penile growth continues postnatally, before, during and after puberty.

## Conclusion

To reinforce HIV transmission prevention in the absence of an effective HIV vaccine, increasing access to VMMC services remains a core strategic intervention to reduce new HIV infections. Expanding access to VMMC services, including pre-operative physical assessment to ascertain presence of physiological and/or anatomical anomalies, could be contributing to increased identification of penile abnormalities among age groups targeted for VMMC. Clients with certain conditions (hypospadias, epispadias, chordee, dorsal hood, abnormal curvature and penoscrotal web) should be referred to specialist urology clinics. In view of the findings of this study, a consistent thorough pre-surgical penile evaluation protocol is recommended to assess and identify abnormalities in all clients before the VMMC procedure is

performed. This will ensure appropriate referral and effective management of identifiable penile abnormalities.

According to this study and other studies, preputial abnormalities are serious causative factors for cystitis, urethritis, pyelonephritis, causing renal damage and renal failure. Therefore, VMMC for abnormalities may preserve the kidney functions, the functions of the urinary system and contribute to a healthy life.

## **Declarations**

### **Ethical approval and consent to participate**

Ethical approval was granted by the Health Sciences Research Ethics Committee of the University of the Free State (UFS-HSD2021/0366/2906). Consent to do an HIV test was obtained prior to the test, and appropriate consent obtained prior to the circumcision procedure.

### **Consent for publication**

Not applicable.

### **Availability of data and materials**

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

### **Competing interests**

The authors declare that they have no competing interests.

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### **Authors Contributions**

MAQ: Provided leadership and oversight on classification of preputial abnormalities, performed the medical circumcisions, and reviewed drafts of the manuscript.

DJ: Conceptualized the study design, classification of the abnormalities, drafting and review of the manuscript.

FD: Conducted the data collation and management and review of the manuscript.

PN: Drafted the initial manuscript and subsequent reviews.

JN: Conducted the data analysis and interpretation and review of the manuscript.

All authors read and approved the final manuscript.

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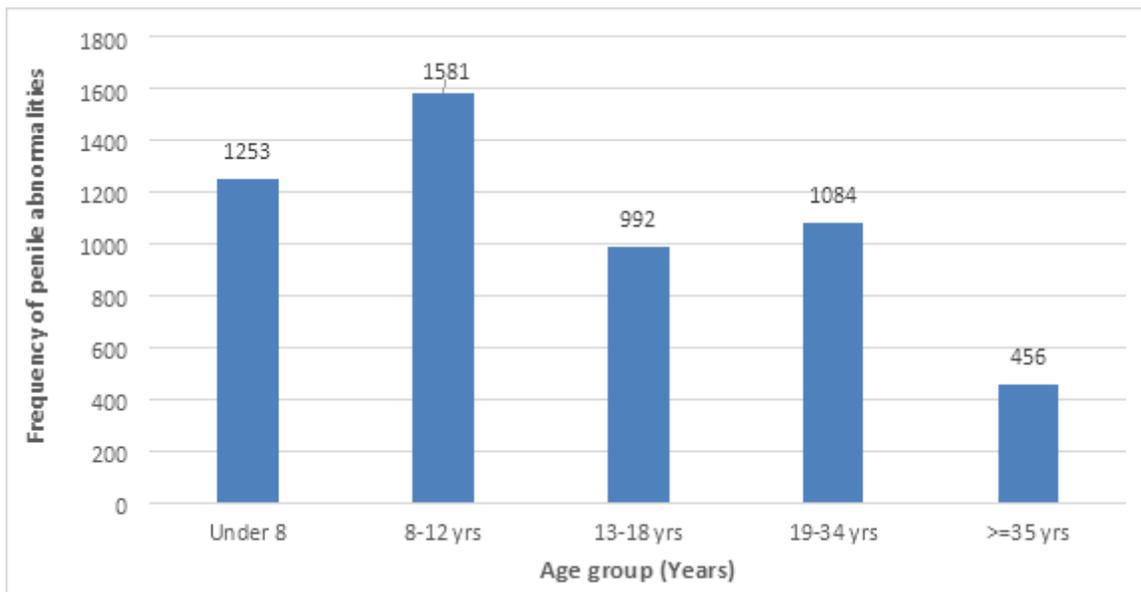
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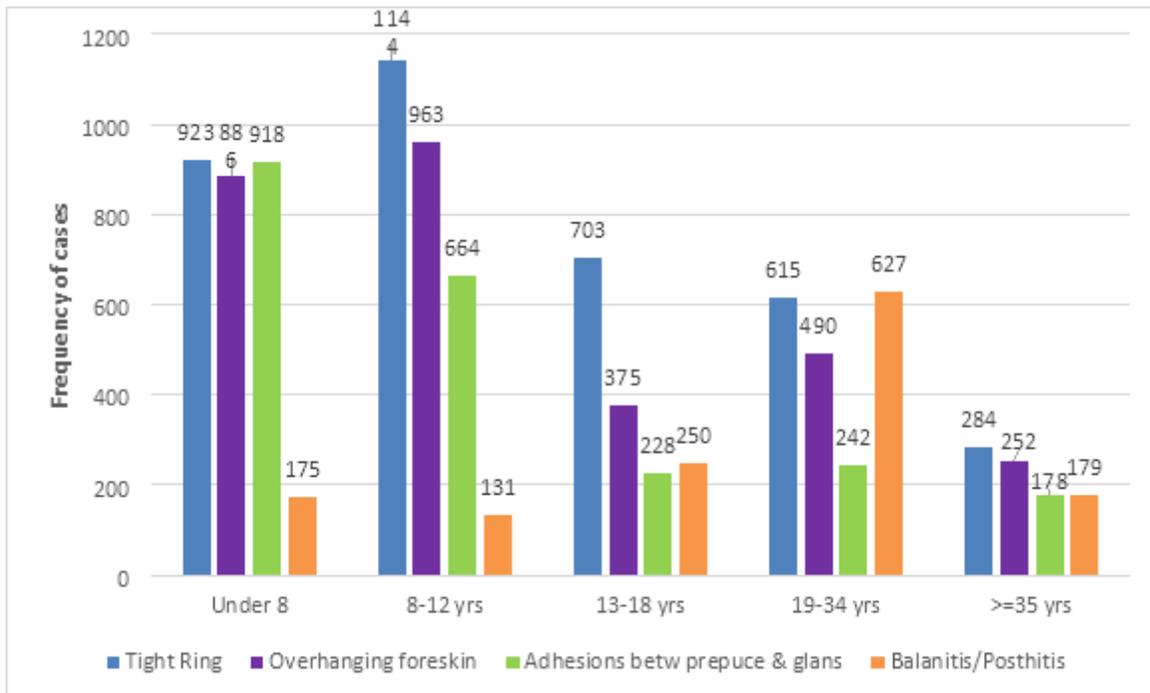
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## Figures



**Figure 1**

Overall distribution of penile abnormalities by age group of the VMMC participants



**Figure 2**

Distribution of specific penile abnormalities cases by age group of the VMMC participants