ABSTRACT

Objectives: To estimate the prevalence of condylomata acuminata/HPV and evaluate associated predictors in infected patients.

Methods: In this cross-sectional and retrospective study, medical records of patients who attended a public health referral center located in Southern Brazil, Parana, between April 2012 and March 2017 were reviewed. Epidemiological, clinical, and laboratory data were analyzed using the chi-square and odds ratio (OR) with 95% confidence interval (CI).

Results: The overall prevalence of condylomata acuminata/HPV in 3,447 patients was 33.1% (n = 1,140). Coinfection of condylomata/HPV with other STI was noted in 23.7% (n = 270) of cases. The population was characterized by a high prevalence (43.8%) in patients aged < 20 years, women (37.4%), white (33.3%), educational level with more than 8 years of study (33.7%), widowed (39.2%), heterosexual (36.7%), and ages between 13 and 19 years at first sexual intercourse (41.1%). A significant association was observed between male sex and multiple partners and between male sex and irregular use of condoms (p < 0.001). The predictors associated with HPV infection were the age group of up to 29 years (OR 2.0, 95% CI 1.3—3.7, p < 0.013) and homosexual/bisexual (OR 0.2, 95% CI 0.12—0.66, p = 0.003).

Conclusion: The findings showed a high prevalence of condylomata acuminata in a public health center study, with emphasis on the age range below the third decade of life and sexual behavior predictors. These predictors are important for the determination of preventive measures against the transmission of infection and the development of cancer.
INTRODUCTION

Human papillomavirus (HPV) is the most common sexually transmitted infection (STI) in many countries. To date, approximately 200 genotypes of HPV have been identified; among them, 40 can infect the human anogenital tract. Genotypes are categorized as low and high risk for developing malignant lesions. Fifteen types were classified as high risk (16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68, 73, and 82); three were classified as likely to be high risk (26, 53, and 66), and 12 as low risk (6, 11, 40, 42, 43, 44, 54, 61, 70, 72, 81, and CP6108). These anogenital HPVs are associated with a broad spectrum of diseases, such as cervical, vaginal, vulvar, anal, perianal, and colorectal cancer, as well as benign proliferative lesions such as anogenital warts or condylomata acuminate.

Globally, condylomata acuminate corresponds to an STI that affects both sexes and is associated with significant morbidity and personal emotional distress. Approximately 95% of cases occur due to genotypes 6 and 11 of HPV1-10; however, approximately one-third of genital warts have multiple HPV types, including coinfection with oncogenic types11. HPV infection is a common adversity in global public health and generates large health, social, and economic consequences in many countries. Approximately US$200 million is spent each year to treat condylomata in the United States, which is often ineffective12. HPV represents the main transmission rate and the population in developing countries being the most affected. More than 50% of sexually active people have been estimated to be infected with HPV at least once in their lifetime14.

The distribution of viral genotypes varies among different populations, and infection rates are influenced by geography, age, sexual history, coinfections, immune status, and genetic factors. Its incidence and general prevalence are not widely known because HPV infection is not a compulsory notification disease15. In the United States, in 2008, a prevalence of 79.1 million cases and an incidence of approximately 14.1 million new cases were estimated16. A review on middle-aged women (35-50 years) showed that the prevalence of HPV differed in geographical regions: Africa (~20%), Asia/Australia (~15%), Central and South America (~20%), North America (~20%), Southern Europe/Middle East (~15%), and Northern Europe (~15%)17, and another review showed a worldwide prevalence of infection in women at all ages of 11.7%, with the highest peak among those aged under 25 years and high prevalence in Sub-Saharan Africa, Latin America and the Caribbean, Eastern Europe, and Southeast Asia (24%, 16.1%, 14.2%, and 14%, respectively)18. In Brazil, the overall prevalence of HPV infection among women, due to cervical cytology, ranged from 16.8% to 28.6%19 and varied in asymptomatic young women considering each region’s characteristics, varying from 2.3% to 32.7%20. In men, HPV can be found in 72% of samples in the genital region21.

Epidemiological data on a population affected by condylomata infection can help in the treatment and implementation of prevention and control activities, reducing public health system expenditures and improving the population’s quality of life and preventive actions against the development of neoplastic diseases. The absence of organized and systematized results with broad scope imposes limitations for the planning of control actions21. In this sense, studies are needed that provide information and clarify the frequency and distribution of infection in different regions of the country and worldwide. Therefore, this study estimated the prevalence of condylomata acuminate/HPV and the predictors associated with the infection in patients with a public health referral service in Brazil’s southern region.

METHODS

A cross-sectional and retrospective study was conducted with patients attending a referral center for diagnosis, treatment, and follow-up of infectious and parasitic diseases located in the municipality of Cascavel, state of Paraná, Southern Brazil called Centro Especializado em Doenças Infecto Parasitárias (CEDIP). This reference center belongs to the public Unified Health System (Sistema Único de Saúde), the public health system established in Brazil serves 25 municipalities in primary care, with an estimated population of 502,59122. The subjects of the survey were all patients referred by physicians from municipalities covered or who accessed the CEDIP service for diagnosis, monitoring, or treatment from April 1, 2012 to March 31, 2017. The study was reported according to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines (S1 STROBE Checklist)23.

For the diagnosis of condyloma / HPV, the syndromic approach should be considered, based on signs and symptoms, and institute immediate treatment without waiting for results of confirmatory tests24. Thus, the clinical characteristics of the patient were observed, and the visualization of suggestive lesions was considered and validated by the medical team.

Sociodemographic information and other relevant risk factors were collected through interviews conducted by trained nurses and physicians using a structured and pre-tested questionnaire, which was part of the medical records. Data of the following predictor variables were collected sex, age, ethnicity, marital status, schooling, behavior, occupation, date of diagnosis, time of onset of symptoms/signs until diagnosis, STI history, STI partner, the number of partners in the last 12 months, reinfection, age of the first sexual intercourse, and use of condoms.

The data collected were organized into a Microsoft Excel® worksheet, and the description consisted of frequency tables and descriptive measures (mean ± standard deviation [SD]). To calculate the effect measure, we used estimated risk (odds ratio [OR]). For calculating confidence intervals (CIs), a confidence level of 95% (α = 0.05) was considered. The data were analyzed in the Statistical Analysis Software® version 9.4. To determine the simple quantitative and prevalence (%) of each variable, only the medical records that had the variable were considered.
The research complied with all guidelines and requirements of Resolution 466/12 of the National Health Council and was approved by the Committee of Ethics in Research in Human Beings of University Center of the Assis Gurgacz Foundation, decision number 1.487.674/2016 (CAAE 36407414.7.0000.5219).

RESULTS

A total of 3,447 people were treated from April 2012 to March 2017, with an overall prevalence of 33.1% (1,140/3,447) for HPV/condylomata. HPV monoinfection was present in 76.3% (870/1,140) of cases and coinfection with other agents with probable or proven sexual transmission was present in 23.7% (270/1,140). For coinfections, cases of condylomata and other infections such as cervicitis, pelvic inflammatory disease, donovanosis, candidiasis, molluscum contagiosum, human T lymphotropic virus, vaginosis, urethritis, epididymitis, balanitis and/or balanoposthitis, and syphilis, were observed. Coinfections were more frequent in women (67.4%). The prevalence of condylomata infection was higher at baseline (47.4%), decreasing with time and reaching 27.9% at the end of the study. According to the study period, the number of patients diagnosed with STI, prevalence of coinfections, and prevalence of HPV are summarized in Figure 1.

The sociodemographic characteristics showed a higher prevalence of condylomata in female patients (37.4%), who were younger than 20 years old (43.8%), had white or brown ethnicity (33.3 and 31.9%, respectively), had more than 8 years of schooling (33.7%), widowed (39.2%), reported heterosexual behavior (36.7%), began sexual life between 13 and 19 years old (41.1%) and used alcohol and illicit drugs (37.7% and 37.6%, respectively). The mean age among the infected patients was 25.8 ± 10.7 years. The predictive variables that showed a statistically significant association with HPV infection were age between 0 and 29 years (OR 2.0, CI 95% 1.2—3.7, p = 0.013) (Tables 1 and 2). About 8.9% (n = 102) of the patients were found to be pregnant or patients who had pregnant partners, 10.0% (n = 100) had a history of STI, 8.7% (n = 99) had STI partners, 17.4% presented reinfection, and approximately 65.4% (n = 742) did not return after treatment. Moreover, 85.2% (n = 819) of the patients sought diagnosis after at least one month after the onset of symptoms, and of these, 11.9% (n = 114) had lesions for more than one year, and these lesions, for the most part, were extensive (Figure 2).

The relationship between sex and condom use with predictor variables (age, marital status, ethnicity, schooling, behavior, number of sexual partners in the last 12 months, and age at first sexual intercourse) is shown in Table 3. Men aged 20 and 39 years (OR 2.9, CI 95% 1.2—7.2, p = 0.012) and single (OR 9.4, CI 95% 9.2—10, p < 0.001) presented a higher risk in acquiring condylomata acuminata, whereas women who reported to have heterosexual behavior (OR 3.4, CI 95% 1.0—12.2, p < 0.048) and married (OR 5.0, CI 95%, p = 0.004) were highly at risk. Individuals who reported heterosexual behavior and did not use condoms were also highly at risk (OR 3.5; CI 95% 1.0—12.7; p = 0.039) of contracting condylomata infection (Table 3).

Table 1 — Baseline characteristics and prevalence of condylomata patients attending in a public health service (Cascavel, PR, Brazil), from 2012 to 2017.

| Predictor variables | Prevalence — n (%) |
|---------------------|--------------------|
| Sex                |                    |
| Female             | 519/1,386 (37.4)   |
| Male               | 621/2,057 (30.2)   |
| Age group (years)  |                    |
| 0-19               | 317/724 (43.8)     |
| 20-39              | 691/2,101 (32.9)   |
| 40-59              | 101/508 (21.6)     |
| ≥ 60               | 22/108 (20.4)      |
| Ethnicity          |                    |
| White              | 385/1,156 (33.3)   |
| Black              | 18/89 (20.2)       |
| Brown              | 450/1,412 (31.9)   |
| Other              | 2/11 (18.2)        |
| Education level    |                    |
| ≤ 8 years          | 969/2,875 (33.7)   |
| > 8 years          | 149/469 (31.8)     |
| Marital status     |                    |
| Single             | 1,029/2,801 (36.7) |
| Married            | 47/194 (24.2)      |
| Divorced           | 13/79 (16.5)       |
| Widowed            | 20/51 (39.2)       |
| Behavior           |                    |
| Heterosexual       | 47/194 (24.2)      |
| Homosexual         | 13/79 (16.5)       |
| Bisexual           |                    |
| Age of first sexual intercourse (years) | |
| ≤ 12               | 21/67 (31.3)       |
| 13-19              | 465/1,130 (41.1)   |
| ≥ 20               | 10/49 (20.4)       |
| Number of current sexual partners | |
| None               | 34/89 (38.3)       |
| 1                  | 462/1,345 (34.3)   |
| 2 or more          | 549/1,542 (35.6)   |
| Current use of any contraception | |
| Yes                | 156/442 (35.7)     |
| No                 | 840/2,291 (36.7)   |
| Use or have already used tobacco | |
| Yes                | 252/725 (34.8)     |
| No                 | 765/2,115 (36.2)   |
| Use or have already used alcohol | |
| Yes                | 49/130 (37.7)      |
| No                 | 968/2,711 (35.7)   |
| Use or have already used illicit drugs | |
| Yes                | 114/303 (37.6)     |
| No                 | 903/2,537 (35.6)   |
Higher risk for condylomata was observed among men who did not use condoms regularly (OR 1.8, CI 95% 1.2–2.7, p = 0.003) or among women who did not use condoms (OR 1.7, CI 95% 1.2–2.5, p = 0.002). Moreover, people with a single partner who do not use condoms or those with multiple partners and use condoms irregularly presented a higher risk of acquiring condylomata (OR 3.4, CI 95% 2.3–5.1, p < 0.001 or OR 2.2, CI 95% 1.4–3.4, p < 0.001, respectively).

**DISCUSSION**

Among the 3,447 patients treated, the prevalence (47.4%) of condylomata/HPV was high in the initial phase of the study, decreasing over time (27.9%). General data in Brazil show that the infection rate is increasing, and in Paraná State, the incidence is 860 cases per 100,000 inhabitants and occupies the fourth position concerning the incidence of cancer (15/100,000)13. Some studies have demonstrated the presence of low-risk genotypes in developing certain types of cancer16, whereas high-risk genotypes are also involved in the development of condylomata17. Cervical cancer is the third most frequent neoplasm in the female population and 16,340 new cases was estimated for the biennium 2016–2017, with risk of 15.85 for every 100,000 women27.

The worldwide prevalence of HPV infection in women is estimated at 11.7%, with the highest peak among those younger than 25 years. The sub-Saharan Africa, Latin America and the Caribbean, Eastern Europe, and Southeast Asia have the highest prevalence worldwide (24%, 16.1%, 14.2%, and 14%, respectively)18. Persistent high-risk HPV infection (mainly genotypes 16 and 18) has been known to be strongly associated with the development of cervical cancer18, whereas the low-risk genotypes (mainly 6 and 11) are related to the development of genital warts19. Although HPV genotypes have not been determined in the patients studied, the characteristics of these patients should be determined due to the presence of high-risk genotypes in patients with condyloma, which show that they correspond to a group who were highly susceptible to developing cancer11.
Table 2 — Condylomata-associated predictors in a public health service (Cascavel, PR, Brazil), from 2012 to 2017.

| Predictor variables                        | Condylomata / n (%) | OR (95% CI)     | p-value |
|--------------------------------------------|---------------------|-----------------|---------|
| Gender                                     |                     |                 |         |
| Female                                     | 520 (45.6)          | 1.3 (0.8—1.9)   | 0.270   |
| Male                                       | 620 (54.4)          |                 |         |
| Age group (years)                          |                     |                 |         |
| 0-29                                       | 872 (76.5)          | 2.0 (1.2—3.7)   | 0.013   |
| ≥ 30                                       | 268 (23.5)          |                 |         |
| Ethnicity                                  |                     |                 |         |
| White                                      | 383 (44.7)          | 1.1 (0.7—1.7)   | 0.623   |
| Others                                     | 474 (55.3)          |                 |         |
| Education level                            |                     |                 |         |
| ≤ 8 years                                  | 272 (24.3)          | 0.7 (0.4—1.2)   | 0.241   |
| > 8 years                                  | 846 (75.7)          |                 |         |
| Marital status                             |                     |                 |         |
| Married                                    | 376 (33.7)          | 1.5 (0.9—2.5)   | 0.118   |
| Others                                     | 739 (66.3)          |                 |         |
| Behavior                                   |                     |                 |         |
| Heterosexual                               | 1,028 (94.4)        | 0.2 (0.12—0.66) | <0.001  |
| Homosexual/Bisexual                        | 61 (5.6)            |                 |         |
| Sex partners in the last 12 months         |                     |                 |         |
| Single partner                             | 492 (47.4)          | 0.8 (0.5—1.3)   | 0.403   |
| Multiple partners                          | 545 (52.6)          |                 |         |
| Age of first sexual intercourse (years)    |                     |                 |         |
| < 15                                       | 138 (27.8)          | 0.9 (0.56—1.36) | 0.553   |
| ≥ 15                                       | 358 (72.2)          |                 |         |

Ref, reference; OR, odds ratio.

It is now well established that persistent high-risk HPV infection is the necessary factor for malignant transformation. However, studies show that the virus alone is not sufficient for developing the disease, requiring the persistence of the virus and contributing factors such as smoking, multiple sexual partners, oral contraceptive use, multiparity, and early sexual life, among others, characteristics observed in patients in this study. In addition, coinfection with other sexually transmitted agents such as herpes virus, cytomegalovirus, Epstein-Barr, and Chlamydia trachomatis, besides immunosuppression by human immunodeficiency virus are also important factors in the development of neoplasms. It is worth noting that reinfection with several types of high-risk HPV may increase the risk of cancer compared to individual infections. Approximately 18% of patients presented with reinfection.

Among the 3,447 patients seen, the prevalence of infection was higher in women (37.5%). Cordeiro et al., show that the number of genital cases is similar between both sexes. However, the group of sexually active women is more affected by infection, mainly due to the development of intraepithelial lesions and due to some biological aspects that make them susceptible to the virus, such as cervical immaturity, inadequate mucus production, and increased cervical ectopy. Although HPV infection is more hostile to women, it is also present in men; however, the number of registered cases is assumed to be low, due to their low demand in the
Table 3 — Association between sex and condom use with predictor variables in patients with condylomata (Cascavel, PR, Brazil), from 2012 to 2017.

| Predictor variables          | Female n (%)    | Male n (%)    | OR (95% CI) | p-value | Do not use condom n (%) | Use condom n (%) | OR (95% CI) | p-value |
|------------------------------|-----------------|---------------|-------------|---------|-------------------------|-----------------|-------------|---------|
| Age group (years)            |                 |               |             |         |                         |                 |             |         |
| 0-19                         | 190 (36.5)      | 127 (20.5)    | 1.2 (0.5-2.9) | 0.732   | 231 (27.9)              | 42 (26.4)       | 1.8 (0.9-3.7) | 0.078   |
| 20-39                        | 258 (49.6)      | 435 (70.2)    | 2.9 (1.2-7.2) | 0.012   | 502 (60.6)              | 105 (66.0)      | 1.2 (0.6-2.3) | 0.668   |
| ≥ 60                         | 58 (11.1)       | 50 (8.1)      | 1.5 (0.6-3.9) | 0.394   | 81 (9.8)                | 12 (7.5)        | 0.8 (0.4-1.6) | 0.557   |
| Marital status               |                 |               |             |         |                         |                 |             |         |
| Single                       | 263 (51.4)      | 414 (68.7)    | 9.4 (2.2-32.9) | <0.001  | 471 (57.9)              | 122 (78.2)      | 4.1 (0.5-31.7) | 0.137   |
| Married                      | 204 (39.8)      | 172 (28.5)    | 5.0 (1.4-17.7) | 0.004   | 300 (36.9)              | 28 (17.9)       | 1.5 (0.2-11.7) | 0.701   |
| Divorced                     | 27 (5.3)        | 14 (2.3)      | 3.1 (0.7-12.9) | 0.099   | 26 (3.2)                | 5 (3.2)         | 3.1 (0.3-30.2) | 0.309   |
| Widowed                      | 18 (3.5)        | 3 (0.5)       | Ref         |         | 16 (1.9)                | 9 (0.6)         | Ref         |         |
| Etnia                        |                 |               |             |         |                         |                 |             |         |
| White                        | 181 (46.4)      | 202 (43.2)    | 2.1 (0.8-5.6) | 0.131   | 270 (44.2)              | 65 (51.6)       | 1.2 (0.4-3.7) | 0.762   |
| Black                        | 6 (1.5)         | 14 (3.0)      | Ref         |         | 14 (2.3)                | 4 (3.2)         | Ref         |         |
| Brown                        | 202 (51.8)      | 250 (53.5)    | 1.9 (0.7-5.0) | 0.195   | 324 (53.1)              | 57 (45.2)       | 1.6 (0.5-5.1) | 0.403   |
| Other                        | 1 (0.3)         | 1 (0.2)       | 2.3 (0.1-48.0) | 0.571   | 2 (0.3)                 | 0 (0.0)         | Ref         |         |
| Education level              |                 |               |             |         |                         |                 |             |         |
| ≤ 8 years                    | 117 (22.8)      | 155 (25.6)    | Ref         |         | 196 (24.0)              | 28 (17.7)       | Ref         |         |
| > 8 years                    | 396 (77.2)      | 450 (74.4)    | 1.2 (0.9-1.5) | 0.274   | 620 (76.0)              | 130 (82.3)      | 1.5 (0.9-2.3) | 0.085   |
| Behavior                     |                 |               |             |         |                         |                 |             |         |
| Heterosexual                 | 493 (98.6)      | 535 (90.8)    | 3.4 (1.0-12.2) | 0.048   | 763 (95.0)              | 144 (92.9)      | 3.5 (1.0-12.7) | 0.039   |
| Homosexual                   | 4 (0.8)         | 43 (7.3)      | 2.9 (0.5-15.6) | 0.186   | 34 (4.2)                | 7 (4.5)         | 3.2 (0.7-15.4) | 0.117   |
| Bisexual                     | 3 (0.6)         | 11 (1.9)      | Ref         |         | 6 (0.7)                 | 4 (2.6)         | Ref         |         |
| Age of first sexual intercourse (years) |     |               |             |         |                         |                 |             |         |
| ≤ 12                         | 11 (4.2)        | 10 (4.2)      | 1.4 (0.3-6.5) | 0.695   | 14 (3.7)                | 2 (2.8)         | 3.0 (0.4-24.4) | 0.280   |
| 13-19                        | 243 (93.5)      | 224 (94.1)    | 1.4 (0.4-4.9) | 0.618   | 355 (94.4)              | 67 (93.1)       | 2.27 (0.6-9.0) | 0.231   |
| ≥ 20                         | 6 (2.3)         | 4 (1.7)       | Ref         |         | 7 (4.17)                | 3 (4.2)         | Ref         |         |

n, number; OR, odds ratio; CI, confidence interval.
health services, mainly due to prejudice, besides the lack of information.

Women older than 40 years had a prevalence of HPV infection of 20.0%. Data from the literature emphasize that women aged over 40 years infected with HPV have a 30-fold increased risk of developing a neoplasm than those younger women. Menopause may influence the reactivation of latent infections acquired early in life due to a gradual loss of immunity or acquisition of new infections from exposure to other sexual partners. The virus reaches widely varying ages, while it focuses on a few specific peaks in women, which increase as the age advances. Men have potentially long-term persistence of HPV infection and a high rate of reinfection. This epidemiological constant of reinfection was verified in this study, with 17.4% reinfected since a greater number were verified in men.

Men are the main propagators of HPV but were mostly asymptomatic and unaware of it, making it difficult to control the infection both in themselves and in their partners, resulting in continuous reinfection. Like cervical cancer, the insistence of HPV infection by genital warts can lead to anal cancer, with 85% of anal cancer cases occurring worldwide being related to this virus, precisely because it is the most common STI. The data reported that women presented a higher rate of HPV coinfection than men (55.24% and 44.76%, respectively) and that 23.68% had HPV and another STI or more, especially those that cause bacterial vaginitis. Chlamydia trachomatis has been very often associated with the development of cervical cancer by its potential in causing intense inflammatory activity, increasing the cervix’s susceptibility, and facilitating infection by persistent HPV. Other important coinfectants, such as herpes virus and cytomegalovirus, have been associated with carcinogenesis due to their presence in cervical neoplasias. In this study, coinfection with other pathogens was found in approximately 24% of condylomata infection cases.

We observed that 60.9% of patients were single, with an infection prevalence of 34.0%. However, an expressive prevalence was also observed in married couples (33.87%). Single individuals are predisposed to contract the infection, probably due to lifestyle. The rate of contamination in married couples may be related to searching for partners outside marriage and can spread more easily to their spouses. This hypothesis can be confirmed by the fact that 52.5% of patients who visited our institution had sexual intercourse with two or more people in the last 12 months, including those with a stable relationship, i.e., married.

The biggest challenge in controlling the transmission chain is that the infection can go unnoticed since 90% of infections can regress spontaneously or remain latent, and an individual remains asymptomatic and undiagnosed for years, but actively spreading the virus. This infection may progress or transform, leading to dysplasias and carcinomas. As a result, persistent infection with at least one type of HPV is a critical factor in triggering carcinogenesis.

Another significant result in our study is that the vast majority of the study population (84.3%) reported that they did not use condoms or did so irregularly, and 85.2% were diagnosed after more than a month from the onset of symptoms. The lack of protection during sexual intercourse is observed in heterosexual and homosexual individuals. Not using condoms or using them irregularly facilitates contamination. Women usually do not worry about STI protection, especially for not using condoms. In this way, they become more vulnerable to having sexual intercourse without condoms since many partners drive a sense of trust and they are unable to impose their desire to prevent STI.

It was verified that 9.0% of patients were in the gestational period or had pregnant partners. The main form of vertical transmission occurs at the time of delivery by genital contamination, mainly due to genital warts or intraepithelial lesions.

This study had some limitations. First, some information in the patient’s records was missing, minimizing the comparison of the predictors. Also, epidemiological data were limited, and underreporting of STI cases was high in Brazil, making it challenging to analyze the prevalence and compare it. However, our results are useful and may help with planning policies and clinical care in patients with STI.

CONCLUSION

In conclusion, our findings demonstrate a high prevalence of HPV/condylomata in the study population. These data justify the implementation of efforts for adequate follow-up in carrier patients. Individuals up to the third decade of life, with at least eight years of formal education and heterosexual behavior, were the most important predictors for determining preventive measures in the transmission of infection and the development of cancer.

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