

REVIEW ARTICLE

Association of Socio-Medical Characteristics with Risk of Human Papilloma Virus Infections among The Females: A Review article

Mallika F. Vhora¹ and ²Vipul Gurjar.

PhD Scholar, Sumandeep Vidhyapeeth Deemed to be University, Vadodara, Gujarat, India.

Dr. Vipul Gurjar, Professor, Dept. of Surgery, SBKSMIRC, Sumandeep Vidhyapeeth Deemed to be University, Vadodara, Gujarat, India.

Corresponding Author's : E-mail: mallv80@gmail.com

ABSTRACT

Persistent Human Papilloma Virus infection is the prime causative factor of cancer cervix and mortality due to carcinoma cervix in females globally. In year 2018 – more than 5 lacs new cases of cancer cervix were diagnosed and more than 3 lacs females lost lives from this disease. Every year almost 5 lacs of females are diagnosed with cancer cervix. It predicts that by year 2050, over 10 lacs females will encounter this killer disease. The knowledge of co-factors causing cervical cancer is spreading increasingly. Almost 75% of the carcinoma cervix are caused by HPV infection - specifically HPV 16 and 18 strains of viruses worldwide. Many other responsible socio-medical characteristics may include early age intercourse, multiple sexual partners, habit of tobacco & smoking, Multiparity, OC pills for more than 5 years & first child birth at young age. The increasing cases of cancer cervix can be decreased by spreading awareness on socio-medical characteristics & prevention on HPV infections, also by arranging large scale screening program to detect the pre-cancerous cervical lesions. [5] This systematic review largely focuses on the socio-medical characteristics linked with infection of HPV and leading to proper understanding of carcinoma cervix. Main aim of the study 1) To epitomize previous research studies, the socio-medical characteristics that are associated with the HPV infection and cancer cervix. 09 electronics data bases searched with compatible keywords. Research Articles were screened by the title and abstract (n=637) and inferred as per the defined eligible criteria (n= 20). Twenty research articles were mentioned in the review study. 60% of the studies clearly suggested that the marriage at younger age or initiation of intercourse at younger age are highly associated with HPV infection among the females, 45% of studies suggested that increased parity or Multiparity is a responsible factors of HPV infection among females. Whereas 30% of the studies suggested that multiple sexual partners or hyper sexual behaviour is responsible factors associated with the HPV infection and eventually develops the cancer cervix. This review provided a contemporary insight of the socio-medical characteristics responsible for HPV infections among females. The main findings of this review are that socio-medical characteristics can play crucial role in causing Human Papilloma Virus infection and cancer cervix, including increased age, increased parity, duration of married life, hyper- sexual activity, multiple sexual partners, pregnancies or deliveries & cigarette smoking etc.

Keywords: Socio-Medical characteristics, HPV Infection, Systematic reviews, Cancer cervix

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INTRODUCTION

Invasive carcinoma of uterine cervix has become the global threat and prevalent cancer diagnosed in females. More than 5.5 lacs new cases of cancer cervix were diagnosed and more than 3 lacs females lost lives from this disease in year 2018. [1] Generally, above 85% cancer cases found in females residing in under developed countries where access to screening procedures, treatment, and Health awareness prevention programs are limited. [2] Persistent infection of HPV (Human Papilloma Virus) is a causative agent of carcinoma of the cervix. [6] The WHO has made an announcement for the cancer cervix elimination globally in May 2018, & > 70 countries participated in campaign. [7] In November, 2020. Global strategy of elimination of cancer cervix preventive strategies including control in future was

released by WHO. For the first time, 194 countries promised together to eliminate cervical cancer in this. [8]

Carcinoma of cervix is 2nd most prime reason of mortality in females behind cancer breast. Carcinoma cervix was commonly diagnosed disease in 28 countries and dominant cause of death in 42 countries, including Sub-Saharan Africa and South Eastern Asia [9]. Topmost cases and deaths rates due to cancer cervix are seen in Africa [10]. In relation to that the rates are 7-10 times are lower in Saudi Arabia, Iraq, New Zealand, Australia and in North America. [11]

Without implementing preventive measures, the novel incidences of cancer cervix is expected to rise from 5.70 lacs to 7 lacs between 2018 and 2030, while the mortality rates is projected to rise from 3.1 lacs to 4 lacs annually.[12] In LMIC, the disease rates are nearly double as high and mortality rates are three times higher as in higher-income countries. Cancer cervix is commonest causes of deaths in India. India's statistics shows that every 8 minutes one woman dies of cancer cervix and every 6 minutes one woman is being diagnosed for cancer cervix.[13] Cancer cervix is the 3rd supreme cause of deaths in India.[14] Difference incidence rates indicates that different components involves in causing the carcinoma cervix. The co-factors are known and consideration of the HPV infection is important but should emphasizes on other socio-medical characteristics of cancer cervix such as Socioeconomic conditions, initiation of early age sexual intercourse, use of tobacco, Extra-marital relationships, early age at the first pregnancy and sexual activity without using a barrier method.[15] The average survival rate is of 5 years. The Length of survival depends on stage and advancement of the cancer cervix on the time of medical diagnosis. The life of females enhances if the cancer cervix is early diagnosed and treated. Most cases of cancer cervix are ruled out at advanced stage and severe consequences decreases the life expectancy of females with carcinoma cervix. A strong responsible factor of advanced level carcinoma cervix is a poor understanding of diagnostic & preventive measures of carcinoma cervix. Per speculum examination is important as the females are not showing signs of disease until it has progressed.[8]

This review aims to examine the association of the socio-medical characteristics with chances of Human Papilloma Virus infection in the females.

REVIEW METHODS

Data searches: A literature search was performed in the following electronics databases: PubMed, CINHALL Plus, Google Scholar, Research Gate, and Science direct, Scopus, Sodhganga, WOS, and MEDLINE were included to search the literature for all publications from 2000 to March-2021.

Key words: Socio-Medical characteristics, HPV Infection, Systematic reviews

2. Search strategy:

Inclusion criteria:

"PICO" framework is used for the inclusion and exclusion criteria for articles selected

PICO framework

P: - Population: Studies must have been collected on asymptomatic females aged 15 to 70 years.

I: - Intervention: Studies must have been implemented any intervention to examine the risk of HPV infection.

C: - Comparison: Studies must have Randomized Control Trials, Observational studies, Cross sectional surveys, Case-control studies & Pre experimental studies.

O: - Outcome: Studies must have included the risk of developing HPV infection, RCTs, Observational studies, exploratory studies etc.

The research articles which directly belongs to socio-medical characteristics and risk of developing HPV infection.

The articles which are easily available online and full texts are available.

The studies which are carried out in English language.

Exclusion criteria:

The studies which are duplicate and result are ambiguous.

The studies which are conducted and published before 2000.

The studies which are published without ISSN number journals.

The studies which are published in local languages.

The studies in which only abstracts are available.

The studies which are not available on journal database

Study Selection:

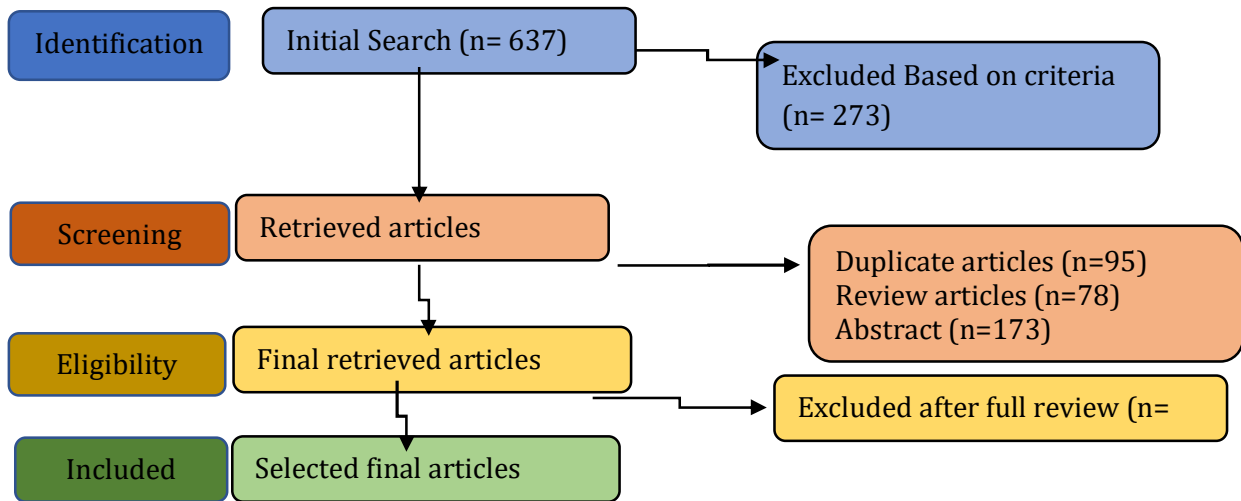


Figure: 1- Flow diagram of Search Strategy with reasons of exclusion

To start with search engines total 637 articles were searched: from that 273 research articles were removed bases on exclusion criteria. Therefore total included articles were 364 among all 95 duplicate research articles. 78 review articles and 173 research abstracts were removed. Final included research articles were 78: among them 58 full research articles were excluded based on inclusion criteria. Finally 20 articles were included in the review.

RESULTS

Table1: Summary: Characteristics of all included research studies (n=20)

| Article/ Ref No. | Study Title | Country | Study Type | Sample | Methodological aspects | Findings |
|------------------|--|----------------|--------------------------------|---|---|---|
| 1/16 | A study conducted by Roura E, castellsague X. et al, on Smoking as a Major risk factors for cervical cancer: results from the epic cohort study” | Spain | Case Control Study | Total 308036 females were selected of age 35 to 70 years | Self-administered standardized questionnaire including socio demographic characteristics were administered among eligible females. History of CIN 3 & CIS positive females were obtained from the Hospital. | The findings of study is confirmation of role of habit of smoking cigar & tobacco as prime risk factor for cancer cervix, along with history of HPV infection. Quitting smoking has relation with two fold reduced risk of cervical cancer. |
| 2/17 | A study conducted by Cooper. D. Hoffman. M. et al. on “Determinants of sexual activity & its relation to cervical cancer risk among South African females.” | South Africa | Cross sectional study | Females with less than age 60 years were selected as samples. Total 524 potential cases and 1541 control cases were enrolled. | Standardized questionnaire administered by face to face interview including socio-demographic, contraception used, reproductive life, STD, Habits etc. | The Study showed that increased sexual activities are directly speculative with infections of HPV. |
| 3/18 | A study done by Misra JS, Srivastava S., et al, on “Risk factors and Strategies for Control of carcinoma cervix in India, Hospital based cytological screening.” | Lucknow, India | Hospital based screening study | Total 36484 females were enrolled for cytological screening up to 35 years. | Under the cytological smear examination, different cervical lesions were identified like erosion of cervix, hypertrophied cervix, suspicious & unhealthy cervix. Any abnormal findings or | Study revealed that certain risk factors are responsible in causing HPV infection & cervical cancer are increasing age, increasing parity, and young age at marriage. |

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| | | | | | HSIL cases –Biopsy were done and findings were associated with the data gathered | |
| 4/19 | A study done by Kour P., Lal M., et al on “Study of the risk factors associated with cervical cancer.” | Jammu & Kashmir, India | Descriptive study | 120 females were recruited with complaints of severe white discharge, Bleeding after intercourse, long term pain in lower abdomen etc. | Per vaginal examination performed, Biopsy were taken of suspicious lesions, Pap test performed along with these, a standard questionnaire introduced seeking information on socio demographic details and reproductive history etc., | This study concluded that multiple pregnancies & initiation of married life at small age, causing HPV infection and cervical carcinoma |
| 5/20 | A study done by Ibrahim, Ahmed. et al. On “Cervical cancer risk factors and feasibility of VIA with acetic acid screening in Sudan.” | Sudan | Cross-Sectional prospective pilot study. | Sample size: Asymptomatic 100 females were selected | Questionnaires on study were introduced on eligible and convinced samples. Gynecological examination were performed. Females were screened for VIA by applying acetic acid. Females with aceto-white lesion on VIA were referred to Colposcopy and further treatment. | 16% of females were positive. And this study suggested that females who have cervix lacerations, female genital mutations, episiotomy and assisted vaginal deliveries have high chances of HPV infection & cancer cervix. |
| 6/21 | A study done by Mhaske M. et al. on “Study of association of some risk factors & Cervical dysplasia/cancer among rural Females.” | Pune, India | Case control study | 462 females were the sample size and pre tested Performa used to interview the samples | Pap smear obtained and collected data were correlated with the positive results of the Pap smear. | This study suggested the significant link with the age of marriage (<17 years), Younger age at 1st pregnancy (< than 20 years), Multiparity and HPV infection. |
| 7/22 | A study conducted by Acosta, Gisele et al. on “Dietary patterns and risk of cervical cancer- A case control study” | Uruguay | Case control study | 536 females as controls with non neo plastic disease were selected and 268 are diagnosed newly and confirmed patients with cancer cervix were selected. 2:1 was control/ case ratio, frequency matched to cases on age & residence. | all the participants were interviewed by 2-3 weeks, structured questionnaire were introduced – socio-demographic data, occupational history, Ht,Wt, H/O cancer in family, habits, sexual history, reproductive history and food preference were collected | This study concluded that there is a relationships between consumption of type foods and beverages and risk of cancer cervix. The red meat food is directly associated with cancer. |
| 8/23 | A study conducted by Remscheid C., Kaufmann AM, et al on “Risk Factors for Cervical Human Papillomavirus Infection and High- | Germany | Case control design with three different groups | Total 237 eligible females were recruited out of which 147 females met the criteria of age 20 to 31 | 25 item questions introduced containing socio-demographic data & quality of life. One group screened for CIN-II, other two groups screened only | Study findings suggested that having history of genitals warts and older age increases the risk of cancer of cervix. Younger |

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| | Grade Intraepithelial Lesion in Females Aged 20 to 31 Years in Germany." | | | years, they were enrolled in group-I those who have CIN-II on histopathology, group II & III had routine cervical screening & no histology investigation. | for HPV by self-sampling and classified as HPV -Ve & +Ve. | stage at 1st sexual relationship and extra marital relationships (many partners) are associated with risk of getting carcinoma cervix. |
| 9/24 | A study conducted by Geetha B. Santhy K.S. et al, on "Sexual risk factors for cervical carcinogenesis - A case control study." | Tamil Nadu, India | Case control study | 200 samples were recruited in the study as patients and controls. | A standardized questionnaire including socio demographic data & sexual risk factors were asked by interview method. | The study suggested that the high risk of cancer cervix are increased age i.e. 40-45 years, HIV infections, OC pills use(>5 years) and period of married life, childhood marriage, Extra marital relationships. |
| 10/25 | A study conducted by Barzanjy, Baran et al, on "Cervical dysplasia assessment & risk factors among females attending the maternity teaching hospital in Erbil, Kurdistan, Iraq." | Erbil, Kurdistan, Iraq | Cross sectional study | Sample size: 2146 females were enrolled in the study. | Questionnaires introduced to obtain the basic data of the samples. Pap smear investigation done using Bethesda Classification system. | The study showed that 248 females had abnormal pap test. And suggested that period of reproductive age, the older ages and longer married life are co-related with higher risk of positive Pap smear findings. |
| 11/26 | A study conducted by Shubhangi, Tulshiram et al, on "Cervical cancer screening risk factors for cervical neoplasia among rural females of Nanded, Maharashtra." | Nanded Maharashtra | Observational cross sectional study | Females attending gynecological OPD were selected for the study. Total 1610 smears were taken and 1485 samples have participated in the study. | Socio demographic details and history were obtained from the samples after consent. Detailed gynecological examinations including Pap smear were introduced among the eligible samples. | 202 smears were showing intra epithelial lesions and 1283 were found normal. This study Age, pre-cancerous cervical lesions, post-menopausal period and multiple parity (>5) were risk for cancer cervix on pap test. High parity is significant and independent risk of cancer cervix. |
| 12/27 | A study conducted by Wang, Zhilian et al, on "Risk factors for cervical intraepithelial neoplasia and cervical cancer in Chinese Females, Large Study in Jiexiy Shanxi Provinces, China." | China | Cross sectional study with 2 phases | 20000 samples of 18 - 65 years were recruited in the study | Eligible samples were given questionnaires on risk factors of Cervix cancer, Females screened for Pap smear, LBC. Samples with Positive findings were undergone Colposcopy with Biopsy. Based on Biopsy results samples allotted to study group /control group and potential risk factors were | Study findings suggested that poor vulval hygiene after physical relationships, decreased folate in diet were linked with the cervix cancer and it might increase the cases. |

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| | | | | | identified | |
| 13/28 | A study conducted by Makuza. J.D., et al, on "Prevalence and Risk factors for cervical cancer & Pre-cancerous lesions in Rawanda." | Rawanda USA | Cross sectional study | 1002 females of age group 30 to 50 years were recruited as samples. Samples were selected from the three different districts. | Standardized questionnaires were introduced, Data were collected from the samples case files, screening performed by doctors and nurses with speculum followed by colonoscopy for biopsy. If no lesion found - VIA is done and VIA positive females underwent cryotherapy/LEEP. Females were called for follow up visit after 3 months. | The study suggested the factors responsible to cause cervical cancer are younger females at first conceiving, sexual activity, and high number of children/parity. |
| 14/29 | A study conducted by Khalaf M., Rasheed F. et al, on "Association between early marriage and other socio medical characteristics with the cervical pap smear results in Iraqi females." | Iraq | Cross sectional survey | 200 samples of post pubertal married phase attending the female health clinic were recruited in the study | Consent obtained and questionnaire were administered including demographic data, life style, reproductive history, occupation followed by clinical investigation and pap smear test. | The study showed that younger age at marriage is the responsible factor of positive pap findings in Iraqi females. |
| 15/30 | A study conducted by Thakur A., Gupta B., et al, on "Risk factors of cancer cervix among rural females of Hilly state." | Himachal Pradesh, India | Case control study | 226 samples were recruited in each case group and control group. Both the groups were matched for age and background | pre designed and pre-tested interview schedule were filled by samples. | The study findings suggested the lack of genital hygiene, younger age at first child birth, younger age at marriage, high parity are the responsible and significant risk associated with the cancer cervix. |
| 16/31 | A study conducted by Bassal R., Schejter E., et al, on "Risk factors for cervical cancer and CIN3 in Jewish females in Israel - Two case control study." | Israel | Two case control study | 40 cases and 40 control were recruited to study the cervical cancer and 99 cases and 79 controls recruited to study the CIN3 | Group-1 Cases and control were recruited form the tertiary hospital. After diagnosis & treatment cases were requested to attend the study and consent obtained, structured tools were introduced. Controls were healthy females attending the regular gynecological clinic and having negative pap smear test. Group-2 CIN3 diagnosed patients were traced at gynecology OPD, asked to take part in the study. Consent obtained and self-administered introduced. Healthy females were in control group having normal pap test in her last 15 years. | Habit of tobacco smoking was observed as a risk factors for cancer cervix & CIN3. Depression & anxiety may be the medicator & not necessarily & direct risk factors. Multiple -more than 5 sexual partners, hypersexual activity, older age, age at first intercourse are found as associated with CIN and cervical cancer. |
| 17/32 | A study conducted | Morocco | Case control | 144 samples of | Standardized | Cases & Controls |

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| | by Berraho M., Amarti-Riffi A., et al, on "HPV and Cofactors for invasive cervical cancer in Morocco. A multicenter case control study." | | study | carcinoma cervix and 288 controls were recruited. Verbal consent obtained. | questionnaires were given including followed by pelvic examination. For cases- HPV-DNA specimen obtained and biopsy done. And for control group only pap smear done. | were described accordingly HPV infections and other factors. This study concluded that the factors of metastasis cancer cervix is multiple parity, education, husband's sexual history & health, physical relationships during menstruation & STDs history. |
| 18/33 | A study conducted by Sharma P., Pattanshetty S., et al, on "A study on risk factors of cervical cancer among patients attending a tertiary care hospital." | Karnataka, India | Case control study | Total 273 participants (91 cases & 182 control) were selected. Information on demographic variables, habits, reproductive history, menstrual history, sexual history, were obtained by using semi structured questionnaires. | All histopathological diagnosed cases of cancer cervix between 28-80 years were included in study are taken as cases. Patients not having cancer cervix in the hospital were selected as controls. Case & control ratio was 1:2 where cases -91 and 182 - controls -total 273 samples were recruited. | This research showed that marital status, alcohol consumption, childhood age at first intercourse, menarche age, parity more than 3 are the major associated risk factors of cancer cervix. In addition to that history of vaginal itching and at least one abortion may associate as a risk factors which can cause cervical cancer. |
| 19/34. | A study conducted by Kashyap N., Krishnan N., et al, on "Risk factors of cervical cancer: A case control study." | 2018 | Case control study | 75 age matched cases & control were selected by Purposive sampling. | Interview Questionnaires introduced. Cases group samples were assessed for the cancer cervix and controls were given any screening procedure. | This research suggested that personal hygiene, old clothe for menstrual hygiene, young age of marriage, lack of genital hygiene after physical relationship with partner, higher numbers of partner's extra marital relations, STDs, genital warts are the associated factors with carcinoma cervix. |
| 20/35 | A study conducted by Sarmiento M., Puerto De Amaya et al, on "Risk factors for cervical cancer and papanicolaou test in marginalized adolescents in Bogota, Columbia ." | Columbia | retrospective cross-sectional study | 889 adolescents samples history papers were used in the study to collect the information | The details of all LBC results carried out in females of 11 to 18 years of age. | Study showed that higher rate of cases especially with the early initiation of physical relations (< 14 years of age), multiple sexual partners in females are correlated with the cancer cervix. |

DISCUSSION AND CONCLUSION

The aim of this review was to find out systematically associated with Socio-medical Characteristics and Risk of Human Papilloma Virus infection among the females. Systematically 20 studies are reviewed encompassing co-factors of persistent HPV infection developing in cervical cancer among the females. Out of 20 studies 11 studies were conducted out of the India and 9 studies were conducted within India.

This systematic review comprises of 10 Case Controlled studies and with different methodologies, 8 cross-sectional surveys and 2 descriptive studies.

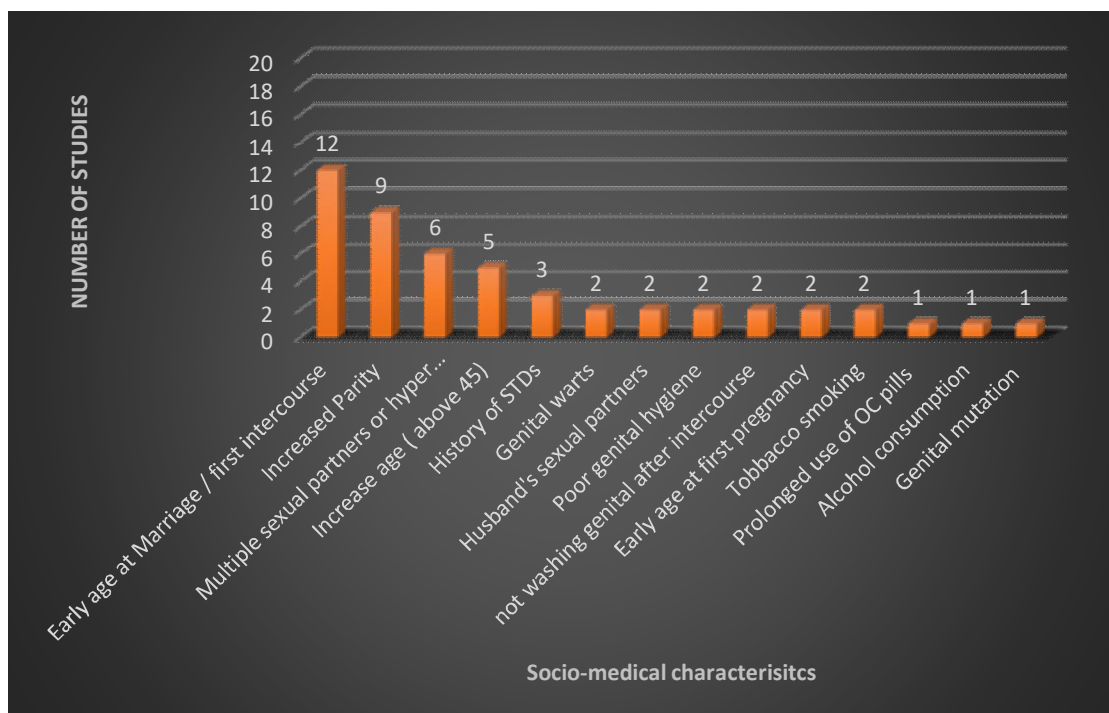


Figure: 2. Association of socio medical characteristics with risk of HPV infection among females

This table shows that among these 20 studies two studies suggested that the early age at first pregnancy is the responsible socio-medical characteristic, another two studies suggested poor genital hygiene including menstruation hygiene is the responsible factor, another two studies reported not washing genitals after intercourse is the responsible factor, other two separate studies reported genital warts and Husbands having extra marital relationships are the responsible factors associated with Human Papilloma Virus infection. Correspondingly out of 20 studies one study suggested that prolonged use of OC pills (over a period of 5 or more years) is the co-factor in developing HPV infection, another different one study reported low intake of folate, increased use of red meat in diet, tobacco, smoking, alcohol consumption, genital mutation/lacerations, intercourse during menstruation, early age at menarche and vaginal itching or abortion are the associated socio-medical characteristics developing the HPV infections and cancer cervix among the females.

The ultimate view behind this study is to identify association of socio-medical characteristics with Risk of Human Papilloma Virus infections among the females. The systematic reviews suggest the need of spreading knowledge on HPV infections, associated socio-medical characteristics, symptoms, preventive measures and screening practices via imparting health education among the community population to prevent the increasing rates of cervical cancer among the females.

LIMITATIONS

Multiple methodologies may curb reliance in the results of the review including : the risk of bias in individual studies due to the lack of control on confounding variables, Small sample sizes, and absence of blinding of samples and outcome evaluators. Ambiguous theoretical framework in many studies.

RECOMMENDATION

Further in depth evaluation is needed to rule out the link between socio-medical characteristics & chances of HPV infection among the females.

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