ABSTRACT

Objectives: To measure the acceptability, beliefs and attitudes on the Human papillomavirus (HPV) vaccine among adolescents and their parents. Methods: Relevant questionnaire-based articles, published in peer-reviewed journals, were retrieved from Medline (through Pubmed and EBSCO) and the Cumulative Index to Nursing and Allied Health Literature (CINAHL) databases. The quality of shortlisted articles was assessed using the CEBMa checklist. Data were extracted and systematically reviewed. Results: Twelve studies (6529 survey participants) were included in the final analysis. The quality of included studies was high (most of the parameters were satisfied according to the CEBMa tool). Of the participants, 187 (2.86 %) were adolescent males, and the rest 6342 (97.14%) were parents of adolescent males. The knowledge of disease severity and benefits of vaccination was low among parents in all studies. The willingness to vaccinate adolescent males was higher among highly educated parents, those with a previously HPV vaccinated female children, and those with a history of recommendation from a physician. Conclusion: A significant gap between actual vaccine uptake and willingness to vaccinate male children was noted in all included studies, mostly due to lack of recommendation by the treating physician. The primary motive to vaccinate sons was the understanding of vaccine benefits and willingness to protect the future partners.

KEYWORDS: Human Papillomavirus Virus; HPV; Human Papillomavirus Vaccine; Adolescents males; Sexual Health.
INTRODUCTION

Human Papillomavirus (HPV) infection is a common, preventable sexually transmitted disease (STD). The HPV virus has a large family of more than 200 different genotypes. Approximately, 40 of the 200 genotypes are transmitted through direct physical or sexual contact.[1] The incidence of HPV infections in men can be as high as in women; however, this fact remains unrecognised widely.[2] Almost 14 million new cases of HPV infection are recorded annually in the United States.[3] Therefore, a vaccine was necessary to protect the population. Gardasil, a quadrivalent vaccine protects against HPV 6, 11, 16 and 18 strains, which cause genital warts and cervical cancer. Cervarix, a bivalent vaccine protects against HPV 16 and 18 strains, which are mainly associated with cervical cancer.[4] These vaccines were approved by the U.S. Food and Drug Administration (FDA) for females in June 2006 and Gardasil was available for males from October 2009.[5,6]

The vaccination for HPV remains low for women, but even lower in males (only 50% of boys get vaccinated in the United States).[5] The national immunization survey has estimated that only 2% of male adolescents in the United States had received any dose of the HPV vaccine by the end of 2010 since the introduction of Gardasil.[7] This could be because it was not listed in the routine vaccination schedule. In 2011, just after the Advisory Committee on Immunization Practices (ACIP) recommendation for the HPV vaccine went into effect, the estimated HPV vaccine coverage among male adolescents in the United States increased to 8.3% (according to the National Immunization Survey-Teen 2011).[5]

At present, the majority of research efforts have been directed towards establishing HPV vaccine implementation, efficacy and side-effects. Several countries have included HPV vaccination in their national immunization programmes for adolescents, though often exclusively for females.[8] In addition, the problem is aggravated with male-to-female HPV transmission that could increase the risk of cancer in females in case the female is not inoculated.[9] Ireland is one of the countries that have established females-only HPV immunization programme, where all girls aged 12 will be offered the HPV vaccine.[10] There is a need for all such countries, including Ireland to promote HPV vaccination for boys as well.

A major controversy during implementing the HPV vaccination is whether it contributes to increased underage sexual activity by giving teenagers a false sense of security.[11] However, an effective way of dispelling misconceptions is through education and awareness, focused
on both parents and adolescents.\textsuperscript{12} Parents’ and adolescents’ acceptance of HPV vaccination could also be influenced by other factors.\textsuperscript{13} A Danish study was conducted in 2010 to assess the parents’ attitudes towards vaccinating sons with the HPV vaccine. It concluded that the main reason for 67\% of parents to vaccinate their boys against HPV was to protect them against cancer. Only 9\% had listed the protection of women from cervical cancer as a sufficient reason to vaccinate their boys.\textsuperscript{14} Therefore, emphasising direct benefits to males could be a strong approach to promoting greater acceptability among males.\textsuperscript{15,16} Positive views from relatives and friends about the vaccine could improve vaccine uptake.\textsuperscript{16,18} Increasing the awareness on the severity of HPV infections, importance of vaccination and parent-son decision making about HPV vaccine could be strongly influenced by healthcare providers.\textsuperscript{19}

A major cause for non-vaccination is the healthcare providers’ failure to sufficiently recommend the vaccine to patients.\textsuperscript{5,20} Despite ACIP permissive guidelines for male vaccination since 2009, barely 15\% of the United States physicians recommend the HPV vaccine to males.\textsuperscript{21} Most physicians agree that a gender-neutral HPV vaccination recommendation would improve public health and raise opportunities to discuss sexual health more openly. Further, mothers are less keen to vaccinate their boys with the HPV vaccine if the vaccine cost over $400.\textsuperscript{15} Moreover, some parents express concerns regarding the safety of the vaccine which harbours the doubts about its efficacy.

The purpose of this systematic review was to measure the acceptability, beliefs, attitudes, views and opinions on the HPV vaccine among adolescents and parents of adolescents. Further, we aimed to review the contributing factors for their opinions because there may be issues that need to be addressed before implementing any national immunization programs.\textsuperscript{22}

METHODS

This work was conducted and reported as per the PRISMA guidelines. The PICOS (Population, Intervention, Comparison, Outcomes, and Study design) strategy was used to break down the study question into concepts to create the search strategy (Table 1). This resulted in identification of two concepts related to our research question, namely; \textit{HPV vaccine} and \textit{adolescent males}. The inclusion criteria were to select studies with any design aimed at understanding one or more parameters like acceptance, beliefs and attitudes of parents about HPV vaccination in men. Adolescent males (aged 10-19 years) and/or parents
of adolescent males were the subjects of choice. Further, data collection should have been carried out based on a survey.

Relevant questionnaire-based articles, published in peer-reviewed journals, were retrieved from Medline (through Pubmed and EBSCO) and the Cumulative Index to Nursing and Allied Health Literature (CINAHL) databases. A combination of relevant keywords was used, namely: “Human papillomavirus” OR “Human papilloma virus” OR “HPV”, “vaccines” OR “vaccinations” OR “immunization”, “parents” OR “mothers” OR “fathers”, “beliefs OR perceptions OR views OR attitudes”. No limitation was set for the language. The date of publications was not filtered because HPV male vaccines were licensed in 2009 and all the references would be recent. Along with the electronic database search, some of the relevant journals were manually searched to identify additional studies.

All the results of literature search were combined in a text file. First, the titles and abstracts were screened. Second, full-texts of relevant articles were obtained for detailed screening. A customised Excel sheet was used to extract data from the included studies, such as year of publication, study design, place of study, characteristics of participants, details of the questionnaire and reported outcomes. Selected studies were critically appraised using the Center for Evidence Based Management (CEBMa) tool for surveys. The studies were graded as of low, medium or high quality. A study with high or medium quality is unlikely to alter the results. A study with low quality raises doubts about the methodology that it has a lot of pitfalls, which significantly lowers the confidence in its results. The outcomes of the included studies were analysed and logically interpreted, considering the corresponding study quality.

**RESULTS**

The literature search retrieved 1217 citations, of which 800 were duplicates and 383 were irrelevant articles. Excluding those, 34 articles were retrieved in full for detailed screening and 22 articles were further excluded. Finally, 12 articles matched our inclusion criteria and were shortlisted for analysis.\[17,23,33\] The selection protocol is depicted as a PRISMA flow diagram in Figure 1.

Table 2 lists the study, patient sample and survey characteristics. The included studies had a total number of 6529 participants, out of which 187 (2.86%) were adolescent males and the rest 6342 (97.14%) were parents of adolescent males. There were 41 (0.63%) mono-sexual, and only 75 (1.15%) participants had prior HPV vaccination, while the rest (98.85%) didn’t
receive prior vaccination. The participants were a mix of parents/mothers of adolescent males whose mean age was 38.46 ± 7.78 years and adolescent males themselves whose age ranged from 5 to 23 years. All were literate who could take self-administered, computer-assisted or web-based surveys. The quality of included studies was good as most of the parameters were satisfied according to the CEBMa tool (Table 3).

The primary outcome of the included studies was to measure the “level of intention” of mothers/parents of adolescent sons to vaccinate their male children against HPV. The factors affecting the HPV vaccination decision included measuring the knowledge, attitude and the effect of education level, marital status, social standard, as well as the number of children. Moreover, social and medical beliefs were measured as factors affecting the mothers’ intentions to vaccinate their sons.

Natan et al. 2017 reported that about 14% of mothers intended to vaccinate their sons, two thirds of which were Arabs and the intention to vaccinate was similar amongst Jewish and Arabs. Most mothers had academic education (77%) and were married (91%) with two children on average. Gutierrez et al. 2013 reported a moderately favourable attitude towards HPV vaccination. Most participants in the study thought that having the vaccine is better despite their belief that it is their choice whether to take it or not. This attitude was much stronger among mono-sexual adults, as compared to heterosexuals. However, the intention to vaccinate was weaker than the attitude towards the vaccine.

According to Donhue et al. 2014, 78.6% of parents had not given the vaccine to their sons. The study reported acceptability of the vaccine among parents of adolescents aged 11-17 years old. The major cause for not having the vaccine was lack of access or recommendation by the physician, concerns about safety or a lower level of education. Shao et al. 2015 reported a 88% lower odds of interest in HPV vaccination in those with inconsistent condom use (Odds Ratio [OR] 0.12, 95% Confidence Interval [CI] 0.014-0.964). Eighty-three percent (83%) of adolescents who underwent routine physical examinations were more likely to be interested in HPV vaccination, compared with those not receiving routine physical examinations (OR 0.11, 95% CI 0.013-0.838).

Schuler and Coyne 2016 reported that just 12% of the parents had a good knowledge about the HPV and its vaccine and another 12% agreed that other parents in the community vaccinate their sons. Most parents (21%) chose not to answer questions about the unknown
long-term side effects of the vaccine and 59% were concerned about its possible long-term side effects. The results of Tisi et al. 2013 showed that 97% of parents were willing to vaccinate their sons, the principal motivation for which was prevention of the diseases, cancerous or not, related to HPV infection.\textsuperscript{[26]} Respondents, unwilling to vaccinate were typically uninformed about the HPV vaccine.

Reiter et al. 2010 reported a low level of knowledge among mothers, as just 43% questions were answered correctly.\textsuperscript{[15]} Mothers reported moderate levels of willingness to get their sons vaccinated against HPV if the vaccine was free (mean=3.3 [possible range 1–5], SD=1.4), with 47% willing to vaccinate. Moss et al. 2015 showed that less than 50% of parents and sons were willing to have HPV vaccine (43% and 29%, respectively).\textsuperscript{[28]} Willing parents and sons anticipated greater regret if the son did not receive HPV vaccine, but later contracted an HPV infection (Parent OR 1.72, 95% CI 1.24-2.40; Son OR=1.51, 95% CI=1.04-2.19) (both $p<.05$).

The results of Clark et al. 2016 study showed that about 51% of parents were unlikely to initiate the vaccine, 39% are likely to vaccinate, but 3% were unlikely to complete, while just 7% completed the course of vaccination.\textsuperscript{[30]} Mortensen et al. 2015 reported that 75% of parents in the UK, Germany and Italy and 49% in France were in favour of HPV vaccination of their sons.\textsuperscript{[31]} Favourable parents wanted to protect their sons from the disease and found gender equality important. Rejecting parents were generally sceptical of vaccines and feared vaccination side-effects. Parents in countries with active vaccination policies (UK and Italy) tended to trust the importance of national vaccination programmes. Parents in countries with passive vaccination strategies (Germany and France) had a greater need for information from health care professionals (HCP) and public health authorities.

Parents included in the study by Muhwezi et al. 2014 were more willing to allow sons to receive the HPV vaccine.\textsuperscript{[32]} Unwilling parents considered HPV vaccination of boys unimportant ($p = 0.003$), believed that only females should receive the vaccine ($p = 0.006$), thought their sons could not contract HPV ($p = 0.010$), did not know about HPV sexual transmissibility ($p = 0.002$), thought that males could not acquire HPV ($p = 0.000$) and never believed that HPV vaccines could protect against HPV ($p = 0.000$).

Bianco et al. 2014 reported that 72.6% considered the vaccine a preventive measure for HPV infection and 55.8% declared that condom use reduces the risk of HPV infection. Seventy-
one percent revealed their intentions to vaccinate their sons, which was significantly associated with perceived benefits of childhood recommended vaccinations, as well as the need for additional information about HPV vaccination. The factors that were associated with a higher knowledge level on HPV prevention included having a higher education level (OR 1.55; 95% CI 1.12–2.16), having received information about HPV infection from physicians (OR 1.71; 95% CI 1.12–2.61), knowledge that HPV is transmitted by sexual intercourse (OR 5.83; 95% CI 1.95–17.44) and that the risk of HPV infection is related to both genders (OR 1.98; 95% CI 1.15–3.42).[33]

DISCUSSION
Following a systemic review to understand the intentions of mothers/parents to vaccinate their male children against HPV, we concluded that parents are more likely to favour HPV vaccination for their sons if they had a higher level of education, better understanding of the side effects and knowledge about the disease severity. Most included studies showed that parental awareness of HPV infection and its vaccine was low. Social beliefs also affected the decision of having the HPV vaccine. Younger mothers who were married were more willing to care for HPV vaccine.

The demographic distribution of HPV-related infection necessitates the intake of its vaccine in early adolescence, when sexual life has not yet been through its most active phases. Therefore, all studies included early adolescents with age ranges between 5 and 23 years old. Being given to adolescents, parental decisions play a pivotal part in the process of initiating, pursuing and completing HPV vaccination. All studies included in this review had one common aim of measuring parental attitudes towards the vaccine, knowledge of HPV infection, level of vaccine acceptance and willingness to give the vaccine to their male children the vaccine. Many studies that compared the parents’ intentions to vaccinate girls to that of their boys showed equal willingness of among parents to vaccinate both their girls and sons.[31,32] According to Muhwezi et al. 2014, parents believed that vaccinating boys was complementary to girls, not to stigmatize females as the only source of STDs.[32]

A positive social attitude towards the vaccination is directly related to parents’ and sons’ willingness to vaccinate.[25] The major motive of parents’ accepting vaccination for their children is their understanding of its protective role against HPV infection.[26] The strongest correlation of mothers’ willingness was understanding that the vaccine may protect their sons’ future spouses or girlfriends from HPV-related disease.[15] In another study, parents
were more willing to give HPV vaccine for their children if they had enough knowledge of its protection to future partners.[28]

Moreover, religious beliefs play a role in improving mothers’ willingness to give their sons the vaccine, even if not for free.[15] A higher compliance was evident among Arabs, as compared to Jewish population. This could be attributed to the religious beliefs of protecting their sons and their future partners.[29] Doctors and nurses’ role in encouraging parents’ willingness is greatly depicted in the results of several studies.[15,29,30] The lack of physician recommendation was the major cause of parents’ unwillingness to vaccinate their sons even after over one year of FDA approval of vaccination to males.[30]

A higher level of education had a positive influence on parents’ acceptance of the vaccine and intention to vaccinate their sons.[33] Mono-sexual males were more aware of the vaccine and its health benefits, as compared to hetero-sexual males. This could be attributed to the involvement of mono-sexual males in practices that had been long linked to development of STDs.[17] Another barrier against HPV vaccination was the increased number of doses to complete the vaccine.[29] Structural barriers also proved to reduce the parents’ willingness to vaccinate their children.[31] Two types of barriers against parents’ vaccine acceptance were recognized as logistic barriers (inability to access vaccine and lack of treating doctor recommendation) and attitudinal barriers (insecurities about vaccine safety and long-term side effects). Most of the parents encountered logistic barriers and were more willing to accept the vaccine with proper awareness and recommendation by the treating doctors.[23]

Limitations and future directions
Few limitations can be pointed out for our review. All the participants from included studies showed a remarkable gap between willingness to have the vaccine and actual vaccine uptake; this gap could not be explained by any of the previous studies. Therefore, larger scale studies should be carried out to further correlate the intention to vaccinate with the actual initiation of vaccination. Another limitation is the lack of studies in the Arabic population which had higher acceptance of the vaccine uptake, but studies are lacking to measure the actual vaccine uptake among this population. However, this review correlates all possible findings available in the literature which proved overall wide range acceptance to the concept of vaccination among male adolescents and provided recommendations for increasing vaccine coverage, including increasing the awareness of parents and adolescent males about vaccine benefits and the encouragement by the treating physicians.
By increasing awareness among parents of adolescent males regarding the health benefits of HPV vaccine and its protective role in preventing rectal cancer and genital warts, physicians could raise parents’ acceptability to vaccinating their male children. Other factor influencing the acceptance are related to social standards and level of education, yet eliminating both logistic and attitudinal barriers could compensate for the lower educational level and social standard. Improving HPV vaccine coverage would be an ideal way to prevent many types of cancers and therefore broad population coverage must be ensured.

Compliance with Ethical Standards
Conflicts of interest: None to declare.

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