



## LETTER TO EDITOR

# Recommendations on Human Papilloma Virus Vaccination to Reduce the Incidence of Cervical Cancer: Yes or no in the Current Situation

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### Dear Editor

Cervical cancer is the fourth most common malignancy in women all over the world.<sup>1,2</sup> Ninety-five percent of cervical cancers occur as a result of a persistent infection of the lower genital tract with the Human Papillomavirus (HPV).<sup>3</sup> Two HPV types-16 and 18-are responsible for 71% of cervical cancer cases.<sup>4</sup> Each year cervical cancer accounts for about 530,000 new cases and 270,000 deaths worldwide and approximately 90% of cases occur in low- and middle-income countries.<sup>5,6</sup> According to the report of Iranian Pathologic-based Cancer Registration Center, 4273 cervical cancer cases have been registered in Iran during 2003-2008 with lowest frequency in 2003 (394 cases) and highest frequency in 2008 (907 cases). In this report, Yazd Province had the highest incidence (14.7 per 100,000) amongst all provinces in 2009.<sup>7</sup>

According to the recommendations, the best way to prevent cervical cancer is to prevent HPV infection especially invasive types in women.<sup>8</sup> As a result, the efforts to develop a vaccine against cancer-causing strains of HPV resulted in development of the first quadrivalent vaccine in 2006 that was approved by the FDA. Then in 2007 the bivalent vaccine and in 2014 the nine-valent vaccine were approved.<sup>9</sup>

Iran is among the countries that have not included the HPV vaccine in the national vaccination program.

Besides, the number of populations who have received HPV vaccine in Iran and mainly in Yazd province in private offices (those who have not followed the national vaccination program) is not clear. Therefore, accurate information is not available on what percentage of the target population has received the vaccine on time.

The results of population-based cancer registry from 2014 to 2016 in Yazd are shown in the Table 1. During these years, the age standardized incidence rate (ASR) of cervical cancer was 2.15, 1.35 $\geq$  and 1.73, respectively.<sup>10-12</sup>

The cancer registration system in Iran was started in 1986 as a pathology-based registration system and continued until 2007. In 2008, in order to improve the quality of the cancer registration process, population-based cancer registration was launched in 20 universities in the country, and since 2014, population-based cancer registration in the whole country has become established. According to the available sources, the age standardized incidence of cervical cancer in Yazd province was 2.04 in 2007, 4.68 in 2008 and 7.14 in 2009. Meanwhile, the incidence in 2009 was more than three times higher than the highest incidence in 2014 (2.15), 2015 (1.35) and 2016 (1.73).<sup>7, 10-12</sup>

Due to the change in the registration system from pathology-based to population-based throughout the country in 2014, it was expected that even if the cervical

**Table 1:** Results of population-based cancer registry on cervical cancer from 2014 to 2016 in Yazd

|                    | 2014  | 2015  | 2016  |
|--------------------|-------|-------|-------|
| Total number       | 11    | 7     | 10    |
| Percent (of total) | 0.53  | 0.34  | 0.9   |
| 25-29              | 0.00  | 0.00  | 1.80  |
| 30-34              | 0.00  | 1.75  | 1.63  |
| 35-39              | 2.56  | 2.38  | 4.30  |
| 40-44              | 3.23  | 3.13  | 5.88  |
| 45-49              | 3.57  | 0.00  | 3.37  |
| 50-54              | 8.70  | 8.33  | 0.00  |
| 55-59              | 10.53 | 5.00  | 4.89  |
| 60-64              | 7.14  | 0.00  | 0.00  |
| 65-69              | 0.00  | 10.00 | 0.00  |
| 70-74              | 12.50 | 0.00  | 23.84 |
| 75-79              | 0.00  | 0.00  | 0.00  |
| 80-84              | 40.00 | 0.00  | 0.00  |
| ≥85                | 0.00  | 0.00  | 0.00  |
| Crude Rate         | 2.13  | 1.32  | 1.81  |
| ASR                | 2.15  | 1.35  | 1.73  |

cancer incidence in the population remained without change, the incidence obtained from the population-based registration system would be higher. But the available evidence showed reverse results, so that in years 2014-2016 the incidence was clearly decreased compared to 2007-2009.<sup>7,10-12</sup> The following reasons that might justify this decrease include: better diagnosis and treatment of dysplasia and carcinoma in situ, acceptable condom use among Iranian people for contraception and improving personal hygiene.

One of the current recommendations for preventing cervical cancer in the world is to use the three-dose HPV vaccine. In this regard, it seems necessary to pay attention to some points:

Prescribing a vaccine sustains a significant cost to the individuals and the health system in case of integration in the vaccination system; and on the other hand, considering that it does not take long to enter the market, its safety and efficacy in long term is under question. In one study published on the cost-effectiveness of HPV vaccine in Iran in 2018, it was pointed out that the use of vaccine in the condition of the country at that time did not seem to be cost-effective.<sup>13</sup>

As mentioned above, the incidence of cervical cancer has decreased in recent years. Given that the use of HPV vaccine is not common in Iran and the knowledge and awareness of the people about this virus and the vaccine is very low, it seems that the use of other methods such as sexual health education and using condoms and pap smears which were less expensive than vaccines, can largely justify this reduction.

Although in the past years we have witnessed a decrease in the incidence of cervical cancer, the HPV vaccine has not been a part of Iran's national vaccination program and still is not. There is not available information regarding vaccine use in Yazd province and it does not appear that a significant number of women have been vaccinated in recent years.

Therefore, it seems that the use of HPV vaccine to

prevent cervical cancer is not a perfect reasonable solution in the current situation and identifying more appropriate alternatives and expansion the use of previous strategies lead to significant reduction in the incidence of cervical cancer.

It seems it is not possible to have a single prescription for all regions and it is important to decide whether to vaccinate people in each region based on the prevalence of cancer, access to the vaccine, and the cost of the vaccine. The authors emphasis that the recommendation about the vaccination in this letter is made by them and could not be generalized.

**Conflict of Interest:** None declared.

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