آبله مرغان در ایران:نگاهی به اپیدمیولوژی و واکسیناسیون

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شهریور 1404

Chickenpox History

- اصطلاح "آبله مرغان" ممکن است از کلمه فرانسوی "chiche-pois"(نخود) که به اندازه بثورات اشاره دارد، یا از کلمه انگلیسی قدیمی " "giganبه معنای "خارش" گرفته شده باشد.
- از نظر تاریخی، ریچارد هبردن برای اولین بار در سال ۱۷۶۷ آبله مرغان را از آبله تشخیص داد.Richard Heberden
- در۱۹۵۰: ویروس واریسلا-زوستر (VZV) برای اولین بار توسط اِولین نیکول و توماس هاکل ولر جداسازی شد.
Evelyn Nicol and Thomas Huckle Weller.

Varicella (chickenpox)

Varicella Disease Burden and Varicella Vaccines Jane F Seward, MBBS, MPH
and Mona Marin, MD
On behalf of the SAGE VZV Working Group
WHO SAGE Meeting
April 2, 2014 .

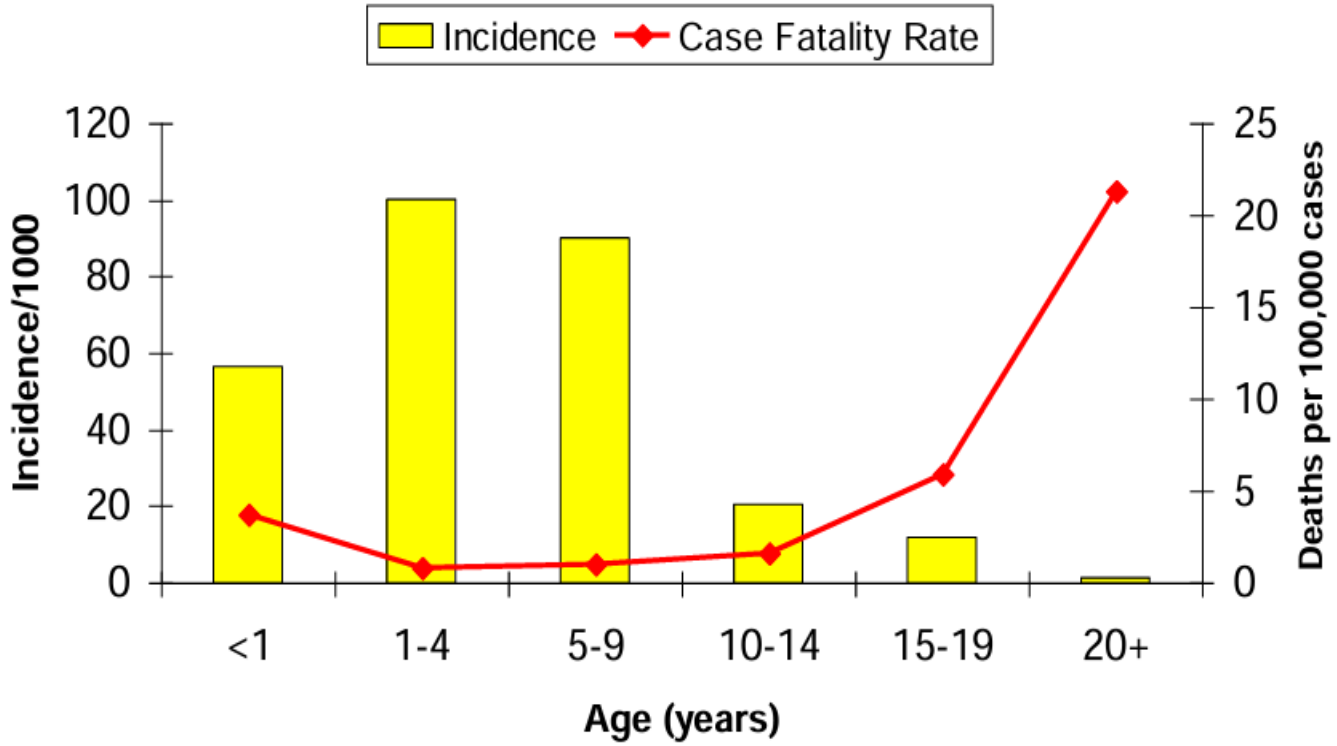
- The World Health Organization estimates:
- annual global burden of varicella to be approximately 140 million cases
- with 4.2 million severe complications requiring hospitalization,
- and 4200 deaths
- In the absence of a universal varicella vaccination (UVV) program, most infections occur during childhood.
- Across Europe, varicella incidence is the highest among children less than 5 years of age and ranges from 7052 to 17,974 per 100,000 population

Varicella (chickenpox)

- Etiologic agent = varicella zoster virus, an α herpesvirus
- Humans only reservoir of infection
  - Primary infection — Varicella (chickenpox)
  - Reactivation — Herpes zoster (shingles)
- Transmission from patients with varicella and herpes zoster primarily via respiratory route following aerosolization of infective viral particles from skin lesions, also direct contact
- Incubation period 10-21 days
- Highly infectious with R_0* ~ 12-18 and household secondary attack rates > 80% (range 61 – 100%)

- R_0= the average number of cases generated by one case over the course of its infectious period in a susceptible population

Varicella Incidence and Case Fatality Rate by Age Group United States, 1990-1994 (pre-Vaccine)



CFR: overall 2-3/100,000 cases US/UK
Children=.~ 1/100,000 Adults = 20-25/100,000 cases

Meyer P et al. JID 2000
Joseph CA et al BMJ 1988

Varicella case fatality rates

Data obtained from the Canadian Notifiable Diseases Surveillance System.

- highest among adults (30 deaths/100,000 cases),
- followed by infants under 1 year of age (7 deaths/100,000 cases) and
- then those aged 1 to 19 years (1-1.5 deaths/100,000 cases).
- In the pre-vaccine era in the United States, adults accounted for only 5% of cases but 55% of the approximately 100 varicella deaths each year.
- In Canada, 70% of the 59 varicella -related deaths in the pre-vaccine years (1987 to 1997) occurred in those over 15 years of age.

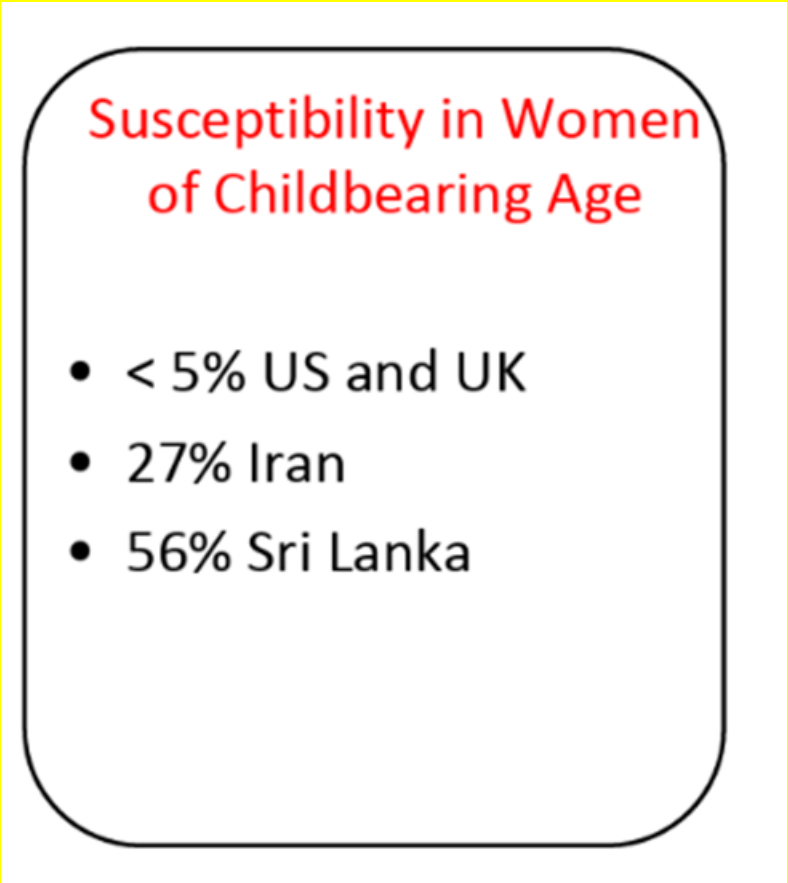
Risk Factors for Severe Varicella and Death

- Age
- Altered immunocompetence
  - HIV/AIDS
  - Childhood leukemia, other cancers and immunosuppressive therapies
- Pregnancy
  - Pregnant women – increased severity?
  - Fetus: congenital varicella syndrome with serious sequelae 0-20 weeks pregnancy
  - Newborn: severe infections if mother has varicella around the time of delivery
- Other: lack of access to health care

Gnann JW. Clin Obstet Gynecol, 2012, Meyer P et al JID 2000, Feldman S and Lott L Pediatrics 1984, Wiegering V et al BMC Pediatrics 2011, Mofenson L et al. MMWR, 2009.

Key Considerations for Special Groups

- **immunocompromised Individuals:?**
- **HIV-Infected Individuals:?**
- .
- **Postpartum Women:**
- Women who are not pregnant and have not had chickenpox should get vaccinated after their pregnancy to prevent exposure to their newborns and others in their household.
- **Household Contacts:**
- Family and close contacts of people with weakened immune systems should get vaccinated to prevent them from spreading the virus to their vulnerable loved ones.
- **Healthcare Personnel:**
- All healthcare personnel who are not immune to varicella should be vaccinated to prevent transmission within the healthcare setting.
- **Susceptible Adolescents and Adults:**
- Individuals who are not immune to chickenpox, particularly those 13 years and older, are recommended to receive two doses of the single-antigen varicella
- Post-exposure vaccination



- Seward JF et al Varicella Zoster Virus: chapter varicella epidemiology 2000; Kilgore P et al 2003; Pourahmad M et al 2010; Kurukulasooriya GM et al 2010; Arunkumar et al 2012; Kudesia G J 2002 12

Varicella and Healthcare Workers

- Nosocomial VZV transmission is a well recognized medical and public health problem
- Sources of nosocomial exposure: patients, health care workers, and visitors with either varicella or herpes zoster
- Health care workers have high risk of exposure and transmission to susceptible patients at high risk of serious or life-threatening complications

Susceptibility profiles HCWs

- < 5% US
- 7% Spain (Catalonia)
- 14-19% Saudi Arabia
- 26% India (students)
- ~ 50% Sri Lanka (students)

Apisarnthanarak A et al Infect Control Hosp Epidemiol 2007, Kilgore P et al J Med Virol 2003; Pourahmad M et al J Clin Virol 2010; Almuneef MA et al Infect Control Hosp Epidemiol 2006, Kurukulasooriya GM et al Asia Pac J Public Health. 2010 Liyanage NP et al Indian J Med Science 2007; Arunkumar et al Am J Ind Med 2012; Kudesia G J Clin Pathol 2002; Fernandez-Cano MI et al Enferm Infec Microbiol Clin 2012, Gustafson T et al AJDC 1984

Vaccination goals

- Achieving high population immunity to control or eliminate infectious diseases
- Protecting individuals from serious illness and death
- Strengthening health systems by reducing the burden of disease.

Estimating the varicella Herd immunity

- Calculating the Herd Immunity Threshold
- **1. Determine the R0 for Varicella:**
- The R0 for varicella can vary by region and time but was estimated at 5.67 in a South Korean study.
- **2. Calculate the HIT:**
- Use the formula HIT = 1 - (1/R0).For example, if R0 is 5.67, then HIT = 1 - (1/5.67) = 1 - 0.176 = 0.824, or 82.4%.
- This means that a vaccine coverage greater than 82.4% is needed to achieve herd immunity.

Factors Affecting the Herd Immunity Threshold :HIT

- **Vaccine Effectiveness (VE):**

The effectiveness of the vaccine impacts the required coverage. Studies show that a one-dose vaccine may be less effective over time compared to a two-dose schedule.

- **Duration of Immunity:**

Live vaccines generally provide long-lasting immunity, but the effectiveness of the varicella vaccine can wane, especially for the single-dose schedule.

- **Vaccine Schedules:**

A two-dose vaccination schedule provides greater and longer-lasting protection than a one-dose schedule.

- **Primary Vaccine Failure:**

The proportion of vaccine recipients who fail to develop immunity after vaccination must be considered

This implies that the **vaccine coverage required to reach the herd immunity** threshold can differ across countries

- **In South Korea, universal one-dose varicella vaccination for children aged 12–15 months has been implemented since 2005, and the coverage attained is 97% in children. Following universal vaccination, varicella incidence declined by 67% over a 10-year period**
- **compared to that in Taiwan (82.2% reduction), where the vaccination policy and coverage were similar.**

- **These differences may be due to**
- **the different background varicella incidence and population immunity levels before introducing the universal vaccination program.**
- **VZV transmissibility can be affected by multiple factors, such as contact patterns, social behavior and structure, and environmental factors,- varicella epidemiology may vary across countries.**
- **substantial variation in VZV transmissibility in European countries as the seroprevalence differed from country to country, and the basic reproductive number (R0) ranged between 3.8 and 16.95.-**

Post-exposure vaccination

Advisory Committee on Immunization Practices :ACIP

- ACIP recommends that after being exposed to varicella or herpes zoster, people with no evidence of immunity and who are eligible for vaccination **should** get varicella vaccine.
- Ideally, the vaccine should be given within 3 to 5 days after the person is exposed. This may prevent varicella or make it less severe.
- Even if it has been more than 5 days, the vaccine should still be offered. This will provide protection against varicella if a person is exposed again in the future and the previous exposure did not result in infection.
- People who previously got the first dose should get a second dose at the appropriate time interval.
- Varicella vaccination is recommended for controlling outbreaks. People who do not have evidence of immunity should get a first or second dose as needed.

The American Society for Reproductive Medicine (ASRM) emphasizes

- (VZV) vaccine is contraindicated during pregnancy, and women should be vaccinated before conception to ensure immunity.
- If a woman planning pregnancy has not had chickenpox and is not vaccinated, she should complete the vaccine series and wait at least one month before attempting conception.
- ASRM also advises completing immunizations before pregnancy because many are contraindicated during pregnancy

varicella vaccine

- **The varicella vaccine contains live attenuated virus. Before pregnancy, all adults should be asked about previous varicella infection or vaccination. Those without evidence of immunity or previous infection should receive 2 doses of single-antigen varicella vaccine administered 1 month apart or a second dose if they have previously received only 1 dose. Pregnancy should be avoided for 1 month after vaccination**
- **If exposed to varicella before pregnancy, the vaccine should be administered within 96 hours of exposure, and pregnancy should be avoided.**
- **Pregnant individuals should be assessed for evidence of varicella immunity. Pregnant individuals who do not show signs of immunity should receive the first dose of the varicella vaccine on completion or termination of pregnancy and before discharge from the hospital.**
- **Cases of congenital varicella after immunization have been reported.**

HZ incidence rate with and without VZV vaccine

Sheila Weinmann, Incidence of Herpes Zoster Among Children: 2003–2014 *Pediatrics* (2019) 144 (1): e20182917.

- The study included 6 372 067 children with ≥1 month of health plan membership.
- For the 12-year period, the crude HZ incidence rate for all subjects was 74 per 100 000 person years,
- and the rate among children who were vaccinated was 38 per 100 000 person years,
- which was 78% lower than that among children who were unvaccinated (170 per 100 000 person years; $P < .0001$).
- Overall HZ incidence declined by 72% ($P < .0001$) from 2003 through 2014.
- Annual rates in children who were vaccinated were consistently lower than in children who were unvaccinated.

Incidence of herpes zoster among children vaccinated with varicella vaccine

Tseng, Hung Fu PhD, MPHIncidence of Herpes Zoster Among Children Vaccinated With Varicella Vaccine in a Prepaid Health Care Plan in the United States, 2002–2008.The *Pediatric Infectious Disease Journal* 28(12):p 1069-1072, December 2009. | *DOI:* 10.1097/INF.0b013e3181acf84f

- There were 172,163 children vaccinated, with overall follow-up of 446,027 person-years (Incidence rate = 27.4 per 100,000 person-years, 95% confidence interval: 22.7-32.7). Children vaccinated after age 5 years had a higher but not statistically significant different rate than children vaccinated between 12 and 18 months (34.3 vs. 28.5 per 100,000 person-years). Among children vaccinated between 12 and 18 months, incidence rates gradually increased each year in the first 4 years after vaccination ($P < 0.001$).
- Among the HZ cases, there were 1 (0.7%) case of lymphoid leukemia, 1 (0.7%) case of drug abuse, 16 (11.1%) cases of asthma with 3 or more acute exacerbations, 12 (8.3%) cases of developmental disorders, and 3 (2.1%) cases of psychological or mental disorders

The incidence of herpes zoster in people who have received varicella vaccine

- The incidence of herpes zoster in people who have received varicella vaccine is up to 5 times lower than in unvaccinated people infected with wild-type varicella (48 per 100,000 person-years compared with 230 per 100,000 person-years, in a study of children aged <18 years). However, when herpes zoster does occur in varicella-vaccinated people, up to 45% of cases may be due to vaccine strain virus

Annual incidence of varicella ***zoster*** IRAN

- There are no readily available studies providing the specific annual incidence rate of varicella-zoster virus (VZV) infection in Iran
- Studies often focus on seroprevalence (the proportion of the population with antibodies against the virus) rather than active infection rates.
- However, seroprevalence studies show high immunity in the population (over 78% overall and reaching over 83% in some age groups), indicating a significant number of past infections.

- The sera of 2753 individuals aged 10–18 were tested for VZV antibodies, from those 87.4% were positive. The prevalence was statistically different in four socio-geographic regions ($P<0.001$), varying between 85.24% in West region (mostly mountainous areas with cold climate) to 94.59% in Southeast region (subtropical climate).
- Among variables studied, only age and mean daily temperature of the living area were positively associated with the VZV seroprevalence.
- Our findings show that most Iranians develop immunity to VZV before the age of 10, but a substantial proportion of them are yet susceptible to the infection.
- Therefore, it seems that the best strategy to reduce the burden of the disease is to vaccinate high- risk adults, i.e. those without a history of varicella infection.
- The regional temperature might be the only determinant of VZV epidemiology in Iran

Seroprevalence of Varicella Zoster Infection at Provincial Level in Iranian Adolescents: The CASPIAN-III Study

Seyed Naseredin Mostafavi, Shervin Ghaffari Hoseini,

Arch Pediatr Infect Dis. 2017; 5(4):e61647.

Table 1. Seroprevalence of Varicella Zoster at Provincial Level by Sex, Living Place, and Age Groups: The CASPIAN III Study[a]

Province	Sex			Living Place			Age Group, y			Total	Total
	Boy	Girls	P Value	Urban	Rural	P Value	10 - 14	15 - 18	P Value		
West Azerbaijan	65 (84.4)	61 (91)	0.23	91 (89.2)	35 (83.3)	0.33	51 (83.6)	75 (90.4)	0.22	126 (87.5)	144
Ardabil	78 (79.6)	90 (88.2)	0.09	110 (82.7)	58 (86.6)	0.48	58 (79.5)	110 (86.6)	0.18	168 (84.0)	200
Isfahan	63 (86.3)	49 (77.8)	0.19	82 (83.7)	30 (78.9)	0.51	63 (82.9)	49 (81.7)	0.85	112 (82.4)	136
Tehran	113 (90.4)	98 (86)	0.28	160 (87.9)	51 (89.5)	0.74	75 (88.2)	136 (88.3)	0.98	211 (88.3)	237
Khorasan Razavi	69 (87.3)	66 (83.5)	0.49	102 (88.7)	33 (76.7)	0.06	44 (74.6)	91 (91.9)	0.011	135 (85.4)	158
North Khorasan	54 (91.5)	47 (82.5)	0.14	35 (81.4)	66 (90.4)	0.16	38 (82.5)	63 (91.5)	0.119	101 (87.1)	116
South Khorasan	52 (92.9)	44 (84.6)	0.17	69 (88.5)	27 (90)	0.82	42 (85.5)	54 (91.5)	0.33	96 (88.9)	108
Khuzestan	72 (78.3)	89 (92.7)	0.004	113 (83.1)	48 (92.3)	0.10	75 (80.6)	86 (90.5)	0.019	161 (85.6)	188
Kurdestan	68 (88.3)	56 (86.2)	0.7	59 (84.3)	65 (90.3)	0.28	64 (86.5)	60 (88.2)	0.75	124 (87.3)	142
Kerman	60 (96.8)	46 (97.9)	0.72	64 (97)	42 (97.7)	0.82	37 (100)	69 (95.8)	0.20	106 (97.2)	109
Kermanshah	97 (85.8)	99 (81.8)	0.40	110 (84.6)	86 (82.7)	0.69	64 (82.1)	132 (84.6)	0.61	196 (83.8)	234
Gilan	55 (91.7)	60 (87)	0.39	71 (91)	44 (86.3)	0.39	54 (90)	61 (88.4)	0.77	115 (89.1)	129
Lorestan	58 (86.6)	70 (89.7)	0.55	123 (87.9)	5 (100)	0.40	56 (82.2)	72 (94.7)	0.007	128 (88.3)	144
Mazandaran	67 (97.1)	65 (100)	0.16	106 (98.1)	26 (100)	0.48	50 (96.2)	82 (100)	0.07	132 (98.5)	134
Yazd	57 (89.1)	61 (84.7)	0.45	67 (88.2)	51 (85)	0.58	57 (86.4)	61 (87.1)	0.89	118 (86.8)	136

Varicella immunity in Iran: an age-stratified systematic review and meta-analysis Abbas Allami, Navid Mohammadi

IRAN. J. MICROBIOL. Vol. 6, No 6 (December 2014) 372-381

Age group	Estimate	95% CI (Lower CL-Upper CL)	N of studies	Total sample
1-5	21.96%	(10.83-33.09)	3	448
6-10	42.09%	(33.57-50.62)	5	704
11-15	59.44%	(46.07-72.81)	6	577
16-20	75.93%	(70.20-81.66)	9	889
21-25	80.23%	(75.31-85.15)	12	1274
26-30	89.54%	(83.62-95.45)	10	983
31-40	85.92%	(79.17-92.68)	8	723
>=40	87.17%	(75.89-98.45)	5	263

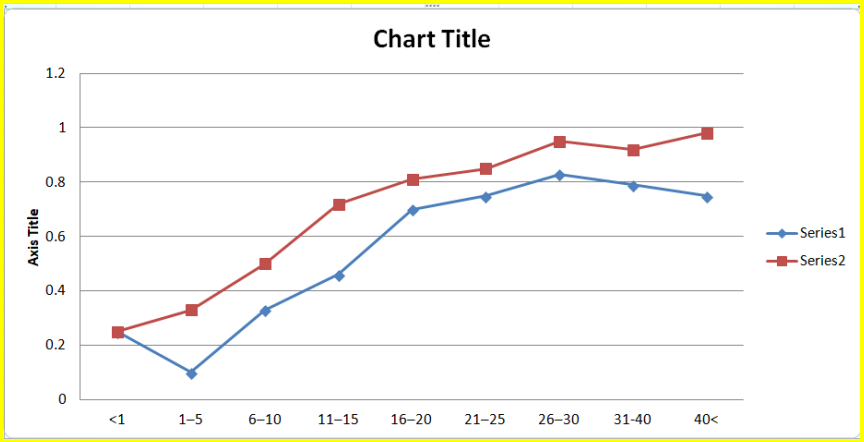
Seroprevalence of Antibodies against Varicella Zoster Virus among Women before Marriage in Yazd, Iran

Zeynali L, Ayatollahi J

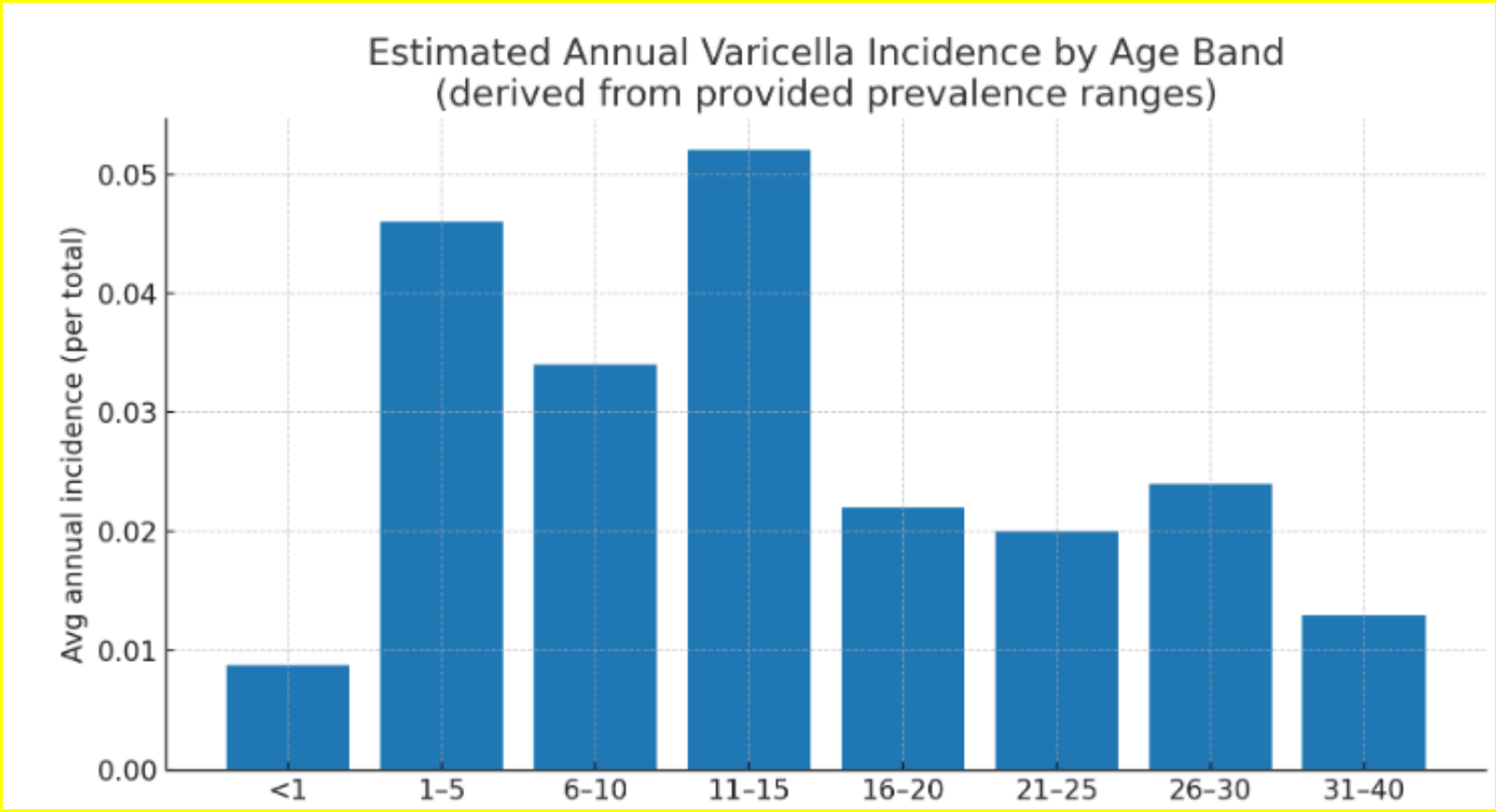
Iranian Journal of Virology, Volume 10, Number 2,3, 2016

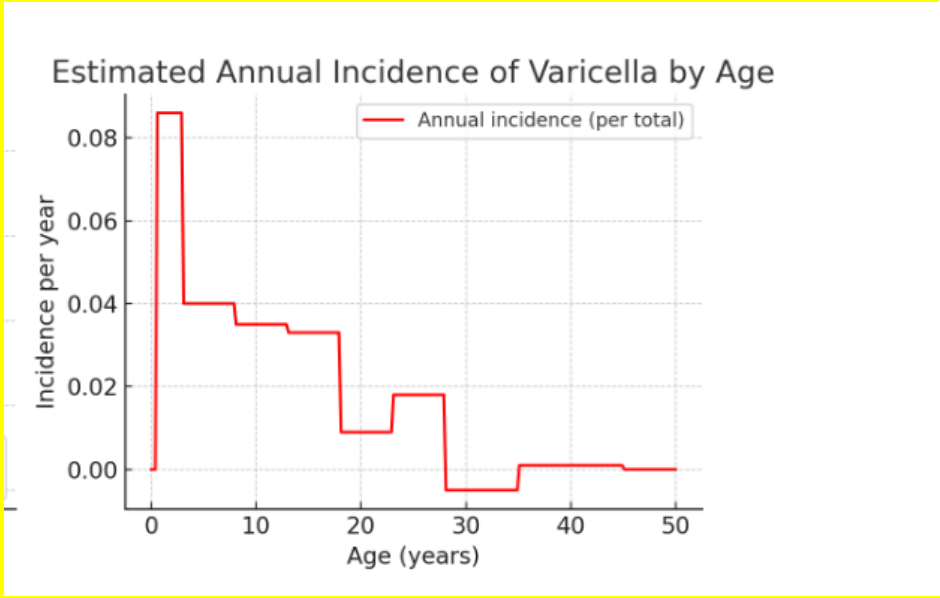
Table 1: Prevalence of varicella antibodies in women before marriage in Yazd

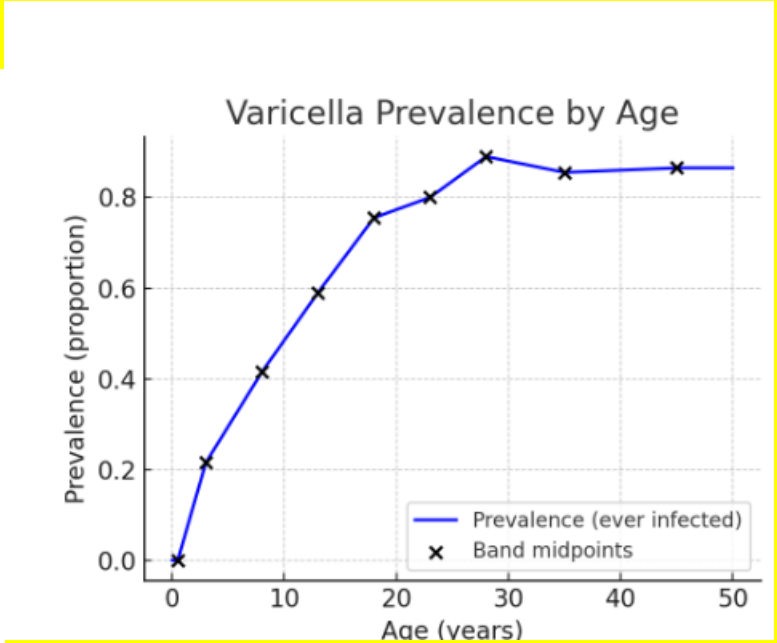
variable		Number	VZV-antibody			P value
			Positive	Negative	Equivocal	
Age (years)	14-23	168	116 (69%)	51 (30.4%)	1 (0.6%)	0.198
	24-33	110	86 (78.2%)	23 (20.9%)	1 (0.9%)	
	34-44	22	19 (86.4%)	3 (13.4%)	0	



- **prevalence curve** for you in words based on your data:
- **<1 year:** Very low, since only about **25%** of infants are susceptible (most have maternal antibodies).
- **1–5 years:** Prevalence rises quickly from ~10% to ~33%.
- **6–10 years:** Climbs further, reaching ~33–50%.
- **11–15 years:** Strong increase, **46–72%** immune by this age.
- **16–20 years:** Around **70–81%**, showing that most teenagers have already had chickenpox.
- **21–25 years:** Increases further to **75–85%**.
- **26–30 years:** High, ~83–95%.
- **31–40 years:** Slightly variable, ~79–92%.
- **>40 years:** Very high, **75–98%**, with only a small fraction of adults still susceptible.
- The curve starts very low in infancy, rises steeply in childhood, reaches **~70–80% by late adolescence**, and approaches saturation (>90%) in adulthood.


Estimated Annual Varicella Incidence by Age Band
(derived from provided prevalence ranges)
Avg annual incidence (per total)
0.00
0.01
0.02
0.03
0.04
0.05
<1
1–5
6–10
11–15
16–20
21–25
26–30
31–40


Estimated Annual Incidence of Varicella by Age
Annual incidence (per total)
Incidence per year
0.00
0.02
0.04
0.06
0.08
0
10
20
30
40
50
Age (years)


Varicella Prevalence by Age
Prevalence (proportion)
0.0
0.2
0.4
0.6
0.8
0
10
20
30
40
50
Age (years)
Prevalence (ever infected)
Band midpoints

Incidence (proportion of each age band infected per year)

- **<1 year:** Very low (~1.5% per year), because most infants are still protected by maternal antibodies.
- **1–5 years:** Peaks here, about **4–5% per year** of all children in this band get infected.
- **6–10 years:** Still high but declining, ~3–3.5% per year.
- **11–15 years:** Slight bump again (~5% per year), reflecting school transmission.
- **16–20 years:** Drops sharply, ~2% per year.
- **21–30 years:** Remains modest (2–2.5% per year).
- **31–40 years:** Further down to ~1–1.5% per year.
- **>40 years:** Very low (~0.3% per year).

So, the **incidence curve rises after infancy, peaks in early childhood, stays moderately high through school years, and then declines steeply in adulthood**.

Absolute number of new cases (because of large population in each band)

- **1–5 years:** Contributes a very large share of cases (~330,000 per year).
- **6–10 years:** Also large, ~220,000 per year.
- **11–15 years:** About 290,000 new cases per year.
- **20–30 years:** Surprisingly big contribution (~300–400,000 total per year) just because so many people are in this age range, even though incidence per person is lower.
- **>40 years:** Contributes only ~60,000–70,000 cases per year, very small compared to children.

Overall picture:

- **The incidence curve (risk per person) is highest in childhood (especially ages 1–15).**
- **The case-number curve (absolute cases) has two bulges: one in young children, and another smaller one in young adults (20s), driven by the sheer size of that population group.**