What is The R_0 Number and Clinical Significance in Infectious Diseases?

Enfeksiyon Hastalıklarında R_0 Oranı ve Klinik Anlamı Nedir?

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Question: *What is the R_0 rate and clinical significance in infectious diseases?* **Ceren Baylan, MD**

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R_0 number is also known as *Basic reproduction number* (R zero or R naught in English pronunciation) and is a term used in epidemiology of infections. For an infectious disease, R_0 number shows the average number of secondary cases that develop after a typical patient (transmitted from this patient) in an entirely susceptible society. Although it is called as *Basic reproductive ratio* or *Basic reproductive rate* in some sources, it would be more accurate to call it Basic reproduction number since it indicates a certain number. The R_0 is generally denoted as a number (eg. 2.6) or numerical distribution (eg. 12-18). The main epidemiological triad variables (infection agent, host and environmental factors) are important in estimating R_0 number. Three main variables play a major role in the calculations: a) The time of infection after a person is infected, b) The possibility of contamination after contact with the susceptible person, and c) The intensity and duration of contact. Even if R_0 is specified as a single number or distribution of numbers, it can actually be influenced by a lot of epidemiological features of the infection (such as transmission route, incubation period, infectious period, the rate of immunity in the population), biological features of the infectious agent, socio-demographic variables (characteristics of the environment, patients and healthy individuals). So R_0 can be thought of as an epidemiological summary of many factors. Although R_0 is basically defined for a fully susceptible population for an infectious disase, it can also be estimated by some mixed calculations in cases where there is a certain level of immunity in the community.

If the R_0 ratio is greater than 1; it is predicted that a patient can transmit the disease to more than one person, and over time the disease will spread gradually in the community, and can cause an epidemic. If the R_0 number is less than 1; not every case can transmit the disease proportionally to another person, and the disease will be self-limited, over time ceased, but there may still be new some cases. Diseases with high R_0 value are more likely to spread and create epidemics in society than diseases with low R_0 value. This spreading rate can reach risky outbreaks, especially if adequate measures are not taken in the community. In practice, by saying R_0=3 for

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a disease, it is understood that in a susceptible society, a sick person can transmit the disease roughly and on average to 3 healthy people.

The R_0 simply indicates how many people spread a disease in the community only from a sick person. There is no relationship between the R_0 value and the severity of the disease. Likewise, the R_0 value does not indicate how quickly the disease has spread in the community. For example, for a disease with slow incubation time, or with a long latent infection period (such as tuberculosis), appearances of secondary cases take long time even if the R_0 is high. However, some other diseases with relatively short incubation periods and without latent infections (eg measles or COVID-19) the potential risk of clinical outbreaks or epidemics will be higher.

R_0 values of different infectious diseases differ from each other. It should also be kept in mind that the R_0 value is given on average, even if it is for the same disease, it is not an absolute fixed number, and may vary according to different conditions. R_0 values are reported as on average; 6-7 in diphtheria, 5-100 in malaria, 12-18 in measles, 4-7 in mumps, 5-17 in pertussis, 5-7 in polio, 6-7 in rubella, 2-5 in SARS, 2-3 in influenza (1918 pandemic), 1.5-2 in Ebola, 0.3-0.8 in MERS and 2-5 in HIV/AIDS (with sexual contacts). In seasonal influenza, it was calculated as approximately 1.3. R_0 is generally found higher in airborne diseases. R_0 values that calculated and/or estimated for a certain disease may differ in various studies, years, social groups, etc. For example, R_0 rates calculated for measles were estimated between 3-203 (median; 6.7-15.9) in various studies conducted in the last century; in pre-vaccination and post-vaccination era, developed and developing countries, according to normal or epidemic surveillance factors, or taking into account birth rates.

When the number of immune individuals increases, the transmission/spread rate of the disease decreases and the transmission rate of the disease is interupted when it reaches a certain critical level. This condition is called as *herd immunity threshold*. The *herd immunity threshold* can be considered as the minimum vaccination coverage rate required for interrupting the spread of an infectious disease that can be protected by vaccination in the community. The *herd immunity threshold* for a vaccine-preventable infectious disease in regard of the vaccine coverage rate may be different for different diseases. The *herd immunity threshold* was estimated to be 83-94% for measles, 75-86% for mumps, 92-94% for pertussis, 80-86% for polio, 83-85% for rubella.

R_0 values have been estimated in different studies for COVID-19 disease, which has been occurring in the world and in our country for the last 3 months and warned by the World Health Organization (WHO) as a pandemic disease. The COVID-19 R_0 value was found to be between 1.4-6.49 (mean 3.28, median 2.79), by evaluating 12 studies studies published between January and February 2020, especially in China and other countries. WHO estimated it to be 1.4-2.5. In general, it can be said that the R_0 value of SARS CoV-2, which causes current COVID-19 disease, is approximately 2.6. This figure is higher than other serious coronavirus infections, such as SARS and MERS, so it can be said that COVID-19 disease has a much faster potential to spread. When we make a simple scenario, if the R_0 value was accepted as 2.6, it was estimated that a patient with COVID-19 would infect 2.6 people after 1 transmission cycle (after 2-14 days, an average of 5 days of incubation period) and infect 368 people after 7 transmission cycles (average 35 days).

In summary, the R_0 value is a value that can reflect how many people can be infected by the index contagious case, especially for a given infectious disease that is newly emerging or the community is totally susceptible to it. However, it would be appropriate to interpret this figure rationally, by taking account together with other epidemiological factors such as with the agent of infection, host and environmental factors.

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