COVID-19 and Children: From an Epidemiological Perspective

COVID-19 ve Çocukların Etkilenimi: Epidemiyolojik Açıdan Değerlendirmeler

Banu CAKIR

Hacettepe University Faculty of Medicine Department of Public Health, Ankara, Turkey

ABSTRACT

COVID-19, caused by SARS-CoV-2, has rapidly progressed globally started from early days of 2020 and was disseminated to 187 countries and territories by April. As of May 3, 2020, COVID-19 has led to a total of 3,507,442 cases and 245,241 related deaths, globally. Turkey, was successful to delay the first COVID-19 case until March 10, yet, case numbers increased fast, reaching to the top 7th rank in the list of countries with the highest case numbers. It is fortunate that the case-fatality ratio was relatively low, with a somewhat stable course around 2.5%. Somewhat stable course of new case numbers, with an apparent decrease through the end of April led to onset of normalization attempts in the country. The future course of the pandemic will be mainly determined by compliance of the general public with personal hygiene, mask use and social distancing.

Globally, COVID-19-related morbidity and mortality rates are lower among children than in adults. Underlying mechanisms for this difference has not been clarified, yet, may be linked to lower exposure rates among children, their immune response may be different and/or higher rates of asymptomatic cases may have lower admissions/testing among children. However, it is important to emphasize that children are prone to SARS-CoV-2, too and all relevant preventions should be ensured. This issue should also be considered in evaluating potential risk of infection transfer from asymptomatic youngsters to the elderly and/or to those with chronic diseases.

Data on COVID-19-related case numbers and deaths in Turkey have not been published so far for children. This requires urgent consideration for related reporting and novel research activities on health burden of COVID-19 on Turkish children. Success in combating the COVID-19 pandemic requires concurrent efforts for clinical management of patients together with epidemiological studies of available national data and establishment of specific research to provide evidence for national and international preventive interventions. Learnings from this pandemic will provide direct evidence for management of future pandemics, and all related parties should be motivated to prepare detailed reporting of ongoing efforts and their outputs.

Key Words: COVID-19, Child health, Epidemiology, Transmission, Prevention

ÖZ

SARS-CoV-2 virüsünün neden olduğu COVID-19 hastalığı, 2020 yılının ilk günlerinden itibaren hızla yayılarak, Nisan ayı sonunda 187 ülke ve bölgeye yayılım göstermiş; 3 Mayıs 2020 itibarı ile dünyada 3,507,442 vaka ve ilişkili 245,241 ölüme neden olmuştur. Türkiye, ilk vakanın görüldüğü 10 Mart 2020 tarihinden sonra vaka sayılarındaki hızla artma sonucu 50 gün içinde vaka sayısı en yüksek 7. ülke konumuna yükselmiş, ancak bu arada ölüm sayılarını göreceli olarak aşağı sınırlarda (%2.5 civarında) tutmayı başarmıştır. Nisan ayının sonuna doğru vaka sayılarında düzleşme ve aşağı doğru gidiş ile gündelik yaşamdaki kısıtlamaların azaltılması konusundaki çalışmalar başlamıştır. Toplumun kişisel hijyen, sosyal mesafenin korunması ve maske kullanımına uyum düzeyine bağlı olarak salgının ülkemizdeki süreci değişiklik gösterebilecektir.

CAKIR B : 0000-0001-6645-6527

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Correspondence Address / Yazışma Adresi:

Banu CAKIR
Hacettepe University Faculty of Medicine Department of Public Health, Ankara, Turkey
E-posta: bcakir@hacettepe.edu.tr

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Dünya genelinde çocukluk çağında COVID-19 vaka ve ölüm sayıları, yetişkinlere kıyasla daha düşüktür. Bunun altında yatan nedenler çocukların enfeksiyonla daha az karşılaşmaları, bağışıklık sistemi cevaplarının yetişkinlerden farklı olması ve/veya asemptomatik olmaları nedeniyle daha az hastane başvuru/test yapılması kaynaklı olabileceği konusunda yayınlar olsa da sonuçları henüz kesinlik kazanmamıştır. Öte yandan, COVID-19 pandemisinin çocukların yaşamı için de bir risk olduğu kesindir ve bu konuda yeterli önlemler alınmalıdır. Bu paralelde asemptomatik ve sağlıklı görünümdeki çocukların enfeksiyonu taşıma konusundaki tehlike hem topluma yönelik kısıtlamalar planlanırken hem de özellikle yaşlı ve kronik hastalığı olan kişilerin bireysel korunmasında dikkate alınmalıdır.

Türkiye'deki vaka sayıları içinde çocuklara ait yüzdeler ve ilişkili risk faktörleri konusunda yayınlanmış bir bilgi henüz yoktur. Bu konuda yapılacak çalışmalara ivedikle ihtiyaç duyulmaktadır. Pandemi dahilinde bir yandan salgına bağlı hastalık yükü ile başa çıkarken, bir yandan da verilerin detaylı inceleme ve analizlerinin yapılması, literatüre katkı sağlayacak çalışmalar ile ulusal ve uluslararası mücadele planlarına katkı sağlanması değerlidir; bu pandemide öğrenilenlerin detaylı olarak yapılması bundan sonraki pandemiler için kanıta dayalı hazırlık sürecine doğrudan katkı sağlayacaktır ve desteklenmelidir.

Anahtar Kelimeler: COVID-19, Çocuk sağlığı, Epidemiyoloji, Bulaş, Korunma

INTRODUCTION

New Coronavirus Disease (COVID-19), caused by SARS-CoV-2 has evolved rapidly after the first case in January 2020, and has spread to 187 countries and territories globally by the end of April. Globally, a total of 3 507 442 COVID-19 cases and 245

241 related deaths were present on May 3, 2020 (1,2). This new disease was first noticed in Wuhan, China, late in December 2019, following detection of pneumonia clusters of undetected etiology; China reported this new disease to the World Health Organization (WHO) Country Office in China on December 31, 2019. The causative virus was first named as 2019-nCoV and the disease was named as the new coronavirus disease. Later, the nomenclature was revised as SARS-CoV-2 to relate its association with a Severe Acute Respiratory Syndrome and the disease was named as Coronavirus Disease, i.e., COVID-19 (3). WHO announced January 30 COVID-19 as a Public Health Emergency at International level due to rapid increase of case numbers across the World, including different continents, and its human-to-human transmission was clarified. WHO announced COVID-19 as a pandemic on March 11, 2020, when the disease was already present in 114 countries, leading to 18 000 cases and 4921 related deaths (4,5).

Pandemic is a communicable disease distributed to several countries in different continents. An announced pandemic requires several precautions for its spread, all of which could lead to restrictions in international relations, trade, educational activities, human movements including travels, etc. These could explain why WHO hesitated to announce COVID-19 as a pandemic, earlier. COVID-19 is an animal-related disease, similar to Influenza pandemics experienced in the World before. The most recent influenza H1N1 pandemic in 2009 was quite different than seasonal influenza outbreaks, occurring more common in young people, with enormous number of cases and fatality. Pandemic İnfluenza A (H1N1) virus is a mixed version of influenza viruses observed in humans, birds and pigs. It was first observed in Mexico in March 2009 and was further spread to several countries, alarmed by WHO as a pandemic disease on June 11, 2009. The disease started in the southern hemisphere first, and spread to the northern hemisphere by the beginning of winter (6).

Globalization, increased number of international travel and commerce, urbanization, crowded cities, shanty settlements, crowded households, increasing population of migrants, seasonal workers, homeless individuals and victims of political crisis have lead over the years to increase in the proportion of population that is prone to social inequalities, immunity problems, hunger etc., together with the increase in close contact of human beings with animals. All these have paved the way to a novel virus-related pandemic, yet, our recent experienced with COVID-19 revealed that the World was not ready to face a pandemic of such a huge size. Given that nobody is immune to this novel virus, it is not possible to stop transmission of this infection until an effective vaccine is invented and becomes highly available for all. (2). Emergence of this novel virus was first linked to some conspiracy theories; yet, laboratory work has clarified that SARS-CoV-2 is linked with a bat coronavirus. (7). Studies are ongoing to establish the underlying mechanisms and the intermediate host(s) for this new virus, but the scientists have already accepted SARS-CoV-2 as a "natural" virus and claim that similar novel viruses may appear in future years, as well. At this stage, it is essential to study SARS-CoV-2 and COVID-19 in depth, including predictors of infection and related fatality, and to work on developing effective medication(s) and vaccine(s) to eliminate this disease in the shortest period (8,9).

Globally, several institutions and hundreds of scientists have been working on vaccine development, and a few have already passed the first stages of testing in animals. Current treatment modalities include off-label use of several drugs, whilst new drug search is ongoing in several countries (19). Before an effective vaccine or medication is in hand, case numbers are expected to increase till the herd immunity threshold is reached. The threshold will depend on the basic reproductive number (R0) and the effective reproductive number (Re). Herd immunity threshold is expected to be at least 40%; which corresponds to a total case number of 32 million for Turkey, including at least 320 000 deaths (11). This is an unacceptably high toll and, thus,

all countries are trying to mitigate or suppress the pandemic as long as they can.

Similar to that in other pandemics, several population measures were undertaken in all populations, based on evidence in some, or simply as indicated by the health authority in others. In contrary to biomedical ethics, public ethics principles prioritize population's needs and social equity, which may sometimes restrict individual rights (such as, sheltering-in or quarantine measures). As allowed in disaster plans and by legislations, individuals and populations may be obliged to obey some restrictions in routine daily lives. In this context, several public restrictions were introduced to communities, starting early in the pandemic. This included travel restrictions in/out of some cities, closure of schools and public places, obligatory home-stays for those aged 20 years or below and for elderly. Mask use has become obligatory in public places including public transport, as pandemic evolves and normalization is initiated.

Mitigation plans aim stabilizing and decreasing new case numbers, providing some relaxation in social life, but risk groups (such as, elderly and those with chronic diseases) need to be protected to the maximum. Economical, social, mental and occupational consequences of total/partial restrictions need to be balanced with the number of actively infected individuals in the population; it is hard to balance the needs for population health versus losses in other areas of life. So far, Turkey has been trying mitigation methods based on provision of 100% compliance with personal hygiene, social distancing and mask use, with addition of stronger public restrictions, as needed.

In the pandemic, imposing public protective measures for children require a tedious plan to cover short term health effects of COVID-19, with its secondary effects on social life, family relations, educational needs, physical exercise, socialization etc., all of which will ultimately adversely affect their well-being.

Effects of COVID-19 Pandemic on Children's Health

Indicators of health in communicable diseases include incidence rate, attack rate, mortality and fatality rates. Real-time evaluations of health during a pandemic, measures such as new/cumulative case numbers, proportion of asymptomatic cases, descriptive characteristics of cases versus non-cases, the proportion of children among all cases and related deaths are easy to calculate, yet useful (12).

The COVID-19 pandemic initiated an unprecedented collaboration among scientists globally, and scientific publications are evolving rapidly to share experiences and learnings among scientists. LitCovid, a curated, web-based network under PubMed, gathers COVID-19-related publications in one site, enabling scientist to access full text manuscripts, even before completion of peer-reviews (13). In LitCovid, there were 10 528 medical papers published and cited in PubMed; of these, only 18 had a Turkish author as of May. Of all publications, 322 papers included the terms of "child" or "children" in the text. This review is based on literature obtained from LitCovid, and the recent review entitled "Coronavirus disease 2019 (COVID-19): Considerations in children" in UpToDate. Literature on COVID-19 in children is relatively scarce and manuscripts are mainly case reports, case series and descriptive work in type; more work on pathogenesis and treatment is anticipated as the pandemic evolves.

First cases in China led clinicians to consider COVID-19 as a disease of mainly elderly and those with comorbidities, with respiratory symptoms and relatively low fatality. Unfortunately, children were found to be at risk, as well, and can transmit disease to others, even when they are asymptomatic (14). Recent publications revealed that children at any age can get infected and develop disease (15-20). In the study of the Chinese Center for Disease Control and Prevention, based on data from 72.314 confirmed COVID-19 cases, only 1% was younger than 10 years old. Wuhan Children's Hospital in China is the only hospital in Wuhan for children under 16 years. COVID-19 test results in this hospital during the period from January 28 through February 26 revealed test-positivity in 12.3% of all children admitted to the hospital (16). The systematic review of all manuscripts published between January 1 and March 18, 2020, proportion of children in all cases ranged from 1% through 5% (21). In China, infection rate of children is 4%-7% in households where there is at least one COVID-19 case; transmission from children to adults in the household is not high, yet, almost all infections among children are through household contacts with adults. In South Korea, 7.1% of all confirmed COVID-19 cases before April 30, 2020 were aged 19 years or lower (18,22-23). Frequency of COVID-19 varies largely across geographic locations due to variations in exposure rates, effective contact numbers, case definitions, testing criteria and identification rate of (all) cases by the health system in a given location. Despite this finding, it is remarkable that proportion of children among confirmed cases are more or less similar in China, South Korea, Italy and USA. Centers for Disease Control and Prevention in USA (CDC), reported a total of 149 760 COVID-19 cases as of April 2, 2020: Of these, 1.7% were aged 18 years or below, and the majority were those residing in New York and New Jersey (18). Only 10% of the infected children provide a travel history prior to infection and all others are likely to be infected from household members or general population. The mean age of infected children is 11 years (0-17), and 53% of all are males 18,20). In China, the majority of infected children are again males (%57-%60), but the mean age [7 years (1-18)] is younger than that in USA population (14-15,17).

The proportion of youngsters among all COVID-19 cases is not sufficient per se to define the risk of COVID-19 in this population. Variations in definition of childhood in different populations, proportion of children in total population, accessibility to health services, testing criteria, availability of testing may cause bias in direct comparisons of COVID-19 case numbers among youngsters across different populations.

It is more appropriate to calculate age-specific and gender-specific, residence-specific (if possible) incidence rates for international comparisons. Current literature and several web-based COVID-19 dashboards provide 14-day cumulative case numbers, together with case numbers for 100 000 population to make comparisons more reliable (24). In comparisons, the onset of the pandemic in a given country is considered as t=0 for the date of the first notified COVID-19 case and comparisons are established at selected dates following day 0, with cumulative numbers presented out of 100.000/1.000.000 of population in that country. Even within a given country, such as in Turkey, availability and numbers of testing, testing criteria, accessibility and timing of testing may lead to underestimation of the numerator in incidence calculations, thus underestimate the true incidence rate in the population. Thus, all nations should provide information on testing criteria, case definition, validity and reliability of the tests used in reporting their COVID-19-related morbidity rates. Whenever follow-up is possible for selected populations (e.g., health workers, imprisoned individuals or nursing home residents), cumulative incidence rates can be calculated or prevalence-type case-control studies may also enable rate calculations for selected closed populations (25).

Age-specific incidence rates are valuable in defining proneness of children to COVID-19. In USA, distribution of confirmed COVID-19 cases by age groups are 11% among 1-4 years; 15% among 5-9 years; 27% among 10-14 years and 32% among those aged 15-17 years (20). European Surveillance System (TESSy) data of the European Center for Disease Control (ECDC), revealed that of all confirmed COVID-19 cases of 266 393 individuals, proportion of those under 10 years old was 1.1% and that only 2.5% was in 10-19 years old group. Under 18 years old, the male-to-female ratio of COVID-19 cases was about 1 (26).

Studies on age-specific incidence rates and related factors are clearly warranted to clarify whether children are less likely to be exposed to COVID-19 or whether they experience more asymptomatic or less severe disease when they get infected, compared to their adult counterparts. Besides direct effects of COVID-19 on child health, secondary effects through socioeconomic losses are likely to have adverse effects on underprivileged children's lives. (27). Future studies need to investigate such secondary effects upon completion of the pandemic. Intolerance to uncertainty, restrictions to daily routines, being away from school and friends, scare of death or family loss may lead to problems in nutrition and sleep disturbances among children. Long-term quarantines and long-term stay-home obligations may decrease physical exercise and increase addiction to television and computer, as well. Social and mental well-being needs to be supported during this time. Upon completion of the pandemic, children may again need support for returning back to their daily responsibilities and social relations.

Severity of COVID-19 among children

At first glance, COVID-19 pandemic was considered as a disease of adults mainly, and children were considered as being less prone to disease, with a 1-2 weeks of recovery period for those with disease. However, even fatal cases have been observed in children, later in the course of the pandemic (21, 28-34). Severity of infection is the most prominent under 1-year-old children but the underlying reasons are yet to be clarified (21). Comorbidity, e.g., chronic pulmonary disease (including, moderate-to-severe asthma), cardiovascular diseases, immunosuppression have been revealed as a predictor of disease severity among children with COVID-19, yet, this proportion is 23% of all cases (21). Hospitalization is needed for 6%-20% of children with COVID-19, with an indication for intensive care unit (ICU) care in 0.58%-2.00% among children hospitalized in USA hospitals. Similarly, in a study from China, 3 out of 19 children needed ICU care and ventilation; all 3 had comorbidity (18). In a study from Italy, of 1591 children, only 1% needed ICU care. A study of PICU-USA, a total of 106 children were given ICU care over the first 4 months of the pandemic, and only one of these children was lost (35). Scarcity of studies on COVID-19 in children, together with small sample sizes of available studies hinder our ability to command on natural course of COVID-19 among children, and disease severity-related risk factors are not clarified. Cohort studies are clearly warranted for conclusive results.

Several hypotheses on lower severity of COVID-19 among children compared to adult patients have been linked with immune response. In SARS and MERS, the main predictor of disease severity was linked to high viral load. The antibodies formed against the other coronavirus infections in childhood (NL63, 229E, OC43, HKU1) may lead to a decrease in severity of COVID-19 due to cross-reaction. Alternatively, quality and quantity of viral receptors in children may be different than those in adults. The S protein in the viral protein structure determines CoV-2 entrance into the cell. The RBP domain of S1 is involved in receptor binding, thus, dominates the proneness of tissues to Corona viruses. SARS-CoV-2 has been shown to enter human cells via angiotensin-converting enzyme 2 (ACE2) receptors. The high affinity of SAR-CoV-2 to ACE-2, makes organs with high ACE-2 receptors (including kidneys, small intestine, testis and lungs) at risk for damage. If ACE-2 protein formation, distribution and number are different across age groups, the intracellular response to alveolar epithelial cell damage will be less in children, compared to that in adults. Low prevalence of comorbidity in childhood may also explain the lower severity of COVID-19 infection among children. All these hypotheses regarding severity of COVID-19 in children warrant further research for conclusive results (36-39). Of the

728 lab-confirmed COVID-19 cases in children in China, about 55%-60% of the cases had mild-to-moderate disease severity (8). The most severe cases in children are reported in infancy, with a prevalence of severe disease in 1/10th of all COVID-19 cases. Caution is needed in interpretation of studies in children, given the limited quality of data collected during active pandemic period, non-standardized nature of testing and/or treatment modalities, variations in accession rate and time to hospitalization and absence of testing in urgent situations for handling severe diseases. Also, presence of any concurrent viral respiratory infections should be identified. Longitudinal case-series and cohort studies are necessary to answer such situations.

Signs and symptoms of COVID-19 in children

Signs and symptoms of COVID-19 are similar in children to that in adults but are less prominent (8), and the course of disease is milder among children (20). The most common symptoms of COVID-19 are fever and cough, followed by difficulty in breathing (18). Among 291 COVID-19 cases in USA, at least one of these symptoms appeared in 3 out of 4 children with the disease (18-20). COVID-19 may be observed in infancy without any symptoms, but fever. Of the 1491 children hospitalized for COVID-19 in Wuhan Children Hospital, the most common symptoms were cough (49%), fever (42%) and pharyngeal erythema (46%). Less commonly reported symptoms included nasal congestion, rhinorrhea, diarrhea, fatigue and vomiting. Among hospitalized patients, the majority had pneumonia (65%) and upper respiratory tract infection (19%). Remarkably, some children admitted by gastrointestinal symptoms, only (18). Rare symptoms included chills, myalgia, headache and loss of smell or appetite (40,41). Recently, some children with COVID-19 reportedly admitted to hospitals with symptoms resembling toxic shock syndrome and atypical Kawasaki syndrome (abdominal pain, gastrointestinal symptom, myocarditis, etc.). These children had high levels of CRP, erythrocyte sedimentation rate and ferritin (42, 43). In New York, a girl admitting to hospital with fever and rash was later tested positive for COVID-19, and a case-report was published to describe this case. Similar cases appeared also in the United Kingdom, Italy and Spain; all these were reported as hyper immune reactions due to prior infections. Between April 17 and May 1, only in New York hospitals, 15 children aged between 2 and 15 years old were treated with Kawasaki-like syndromes: four of these were COVID-19 test-positive, whilst the other 6 had antibodies against SARS-CoV-2. All children recovered, only one needed , a “hot topic bias” and “increased alertness/ familiarity of physicians” might have led this finding, as well. A severe case with Kawasaki-like syndrome and PCR-positivity for SARS-CoV-2 died in New York, recently. Altogether, this issues needs to be studied further.

Besides milder symptoms of COVID-19 among children, PCR test positivity rates are also lower than that in adults. Among symptomatic children PCR-positivity was 12% and only 16% of children with PCR-positivity had any symptoms (9). These may make infected children act as “super-spreaders” for the elderly in household setting or in close vicinity (45). A thorough clinical examination and testing are necessary for children with contact history and/or symptom; testing should be repeated, if needed; and, schooling should be discussed cautiously in those with contact history, regardless of symptoms. In estimation of herd immunity, the number of children with passed COVID-19, yet, remained undetected should be investigated. Also, the association between symptomatic status and epidemiologic and virological findings deserves to be well studied for clarification of pathogenesis in children.

In Wuhan, of all children with confirmed COVID-19 diagnoses, one-fourth had leucocyte count less than 5.5 x 109/L, in 3.5%, lymphocyte count was below 1.2 x 109/L (8); procalcitonin was high (>46 pg/mL) in 64% and one in every five children C-reactive protein was also high (>10 mg/L). Chest X-rays varied greatly, from no changes to bilateral consolidation (46,47). Of 171 children with confirmed COVID-19, 33% had ground-glass appearance in thoracic CTs, 19% had patchy spots and 12% had bilateral opacities (16,35). Some studies revealed that the majority of radiological changes appeared prior to symptoms (48,49). In 8 children with COVID-19, lung ultrasonography revealed sub-pleural consolidation and B lines (50).

In vitro transmission and risk of breast-feeding

COVID-19 appeared in a variety of different forms in pregnant women, ranging from asymptomatic or mild case status to leukocytosis and consolidation in thoracic tomographies. Two pregnant women with COVID-19 were treated in ICU, yet, the details of their disease status are not known. Scarcity of the number of studies on COVID-19 in pregnant women points at a need for future case-series and/or cohorts for conclusive results (35,51).

Similarly, literature knowledge on possibility of intra-uterine or prenatal transmission is scarce. Some recommends cesarean section when COVID-19 is present in pregnant woman. Yet, vaginal delivery has not been shown to lead to any COVID-19 transmission to the new born, to date. In 30 newborns of COVID-19 mothers have recently been shown to have no virus, yet, a few had perinatal complications and SARS-CoV-2 positivity in their placentae (35).

Transmission of SARS-CoV-2 through breast-feeding has not been studied adequately. Of the 6 breastfeeding mothers with COVID-19, no virus was detected in breast milk, however, close contact of mom and the baby and infected droplets may lead to transmission to the newborn, thus, individual protective measures are needed (52).

COVID-19 and Children: Experience in Turkey

The first COVID-19 case in Turkey was reported on March 11, 2020; seven days later, the first COVID-19 case with a domestic contact was announced by the Ministry of Health (MoH), together with the first COVID-19-related death. Since then, daily media announcements of the MoH have been providing data on numbers of new cases and deaths, those in ICU and patients requiring mechanical ventilation, together with daily test numbers (53). As of May 4, 2020, a total of 1 171 138 PCR test were done; a total of 127 659 cases and 3 461 were detected. Unfortunately, age-specific distributions are unknown.

The national burden of COVID-19 and related death toll need to be investigated further for their associations with related risk factors for providing robust evidence for public preventive measures. In this sense, we need more detailed analysis of national data providing specific distributions of cases by age, gender, residential setting, history of contact, date of diagnosis, and comorbidity. It is important to investigate distributions by date of infection, date of hospitalization, and clinical characteristics for those admitted to hospital. Epidemiologic studies on proportion of children among all cases, percent of those with symptoms and transmission rates among children will be valuable. Effectiveness of treatment modalities and types and frequencies of adverse effects (if any) need to be investigated. All such data will be useful for policy makers to base their decisions on robust evidence and to forecast the future of the pandemic under different scenarios.

In Turkey, following the rapid increase in case numbers, various combinations of public and individual measures enabled a steady state for some time, and daily death numbers decreased to below than 100. This control in numbers was perceived by the majority of population that the *"peak value is reached and the numbers will go down soon*". However, high transmission rates and human-to-human transmission make COVID-19 a hard pandemic to control, unless an effective vaccine is found and becomes available for everyone. Given that nobody is immune to this novel virus, a herd immunity (of about 40%-60% infection for an average R0 value of 2.5-3) means thousands of deaths, which is not acceptable for any country. So far almost 40 000 mutations are reported in SARS-CoV-2, yet, none has led to any significant change in clinical picture. So far, seasonal effects have not affected the course of pandemic, either. Altogether, countries need to comply with strict individual measures (masking, social distancing and hygiene), and public measures tailored to local needs may sometimes need to be strengthened to decrease cases under affordable numbers for the health care system.

Turkey has been successful so far to mitigate the pandemic without causing a shut down in the health system, yet, it is important to consider COVDI-19 as a long-term health problem and all sectors need to excogitate "effective survival methods" in the presence of the pandemic. In the meanwhile, scientists will continue to work on effective medications and vaccine(s), based on evolving literature on pathogenesis of COVID-19 in adults and children. Public messages need to be informative, transparent and uniform . It is important to convey the messages based on concrete evidence, not to evoke a false sense of safety or an unjustified panic in the population. It is important to collect objective, quantitative and comparable data; to provide timely and detailed reporting of available data for policy makers, and to share the novel information with colleagues across the nations. Pandemics cannot be avoided, yet, we can learn from them and use this knowledge to be ready for the upcoming ones.

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