COVID-19 cases

Daily national Covid deaths fall below 100 after 9 months (The Tribune: 20210202)


India registered 8,635 new coronavirus infections in a day, the lowest in eight months, while the daily deaths fell below 100 after almost nine months, according to Union health ministry data updated on Tuesday.

The number of COVID-19 cases stand at 1,07,66,245 and the death toll increased to 1,54,486 with 94 new fatalities, the data updated at 8 am showed.

The number of people who have recuperated from the disease surged to 1,04,48,406 pushing the national recovery rate to 97.05 per cent, while the COVID-19 case fatality rate has dropped to 1.43 per cent.

The COVID-19 active caseload remained below two lakh for the 14th consecutive day.

There are 1,63,353 active coronavirus infections in the country which comprise 1.52 per cent of the total caseload, the data stated.

India’s COVID-19 tally had crossed 20 lakh on August 7, 30 lakh on August 23, 40 lakh on September 5 and 50 lakh on September 16. It went past 60 lakh on September 28, 70 lakh on October 11, crossed 80 lakh on October 29, 90 lakh on November 20 and surpassed the one-crore mark on December 19.

According to the Indian Council of Medical Research, 19,77,52,057 samples have been tested up to February 1 with 6,59,422 samples being tested on Monday.
The 94 new fatalities include 27 from Maharashtra, 17 from Kerala, seven from Tamil Nadu, six from West Bengal, five from Chhattisgarh, four each from Uttarakhand, Haryana and Uttar Pradesh, and three each from Delhi, Karnataka and Puducherry.

A total of 1,54,486 deaths have been reported so far in the country including 51,109 from Maharashtra, 12,363 from Tamil Nadu, 12,220 from Karnataka, 10,856 from Delhi, 10,179 from West Bengal, 8,662 from Uttar Pradesh and 7,154 from Andhra Pradesh.

The health ministry stressed that more than 70 per cent of the deaths occurred due to comorbidities.

“Our figures are being reconciled with the Indian Council of Medical Research,” the ministry said on its website, adding that state-wise distribution of figures is subject to further verification and reconciliation.

**Surgery Knee replacement**

**This alternative surgery may prevent total knee replacement (The Tribune: 20210202)**


Total knee replacement is frequently performed on older patients with end-stage disease and limited mobility.

An underused type of knee surgery in younger patients shows considerable success in reducing the need for total knee replacement, a new study suggests.

The surgery, named high tibial osteotomy, is a knee surgery aimed at younger patients in the earlier stages of knee osteoarthritis, according to the study published in CMAJ (Canadian Medical Association Journ)

“One of its goals is to prevent or delay the need for knee replacement,” said co-author Trevor Birmingham from the Western University in Canada.

“In some ways, it’s like performing a front-end alignment on your car to stop asymmetric wear on your tires and increase their longevity,” Birmingham added.

Knee osteoarthritis is a common cause of pain and disability and puts tremendous burden on health care systems. Total knee replacement is frequently performed on older patients with end-stage disease and limited mobility.
Of the patients in this study getting high tibial osteotomy (643 knees in 556 patients), 95 per cent did not need a total knee replacement within 5 years, and 79 per cent did not get a total knee replacement within 10 years.

Even in patients traditionally not considered ideal candidates for high tibial osteotomy (e.g., women and patients with later-stage disease), about 70 per cent did not get a knee replacement within 10 years.

The procedure is particularly suitable for people who are younger, have less severe joint damage and who may be more physically active.

“Those patients especially contribute to the burden of knee osteoarthritis,” the researchers said.

“There is a treatment gap between exhausting non-operative treatments and appropriateness for joint replacement, resulting in many years of pain, lost productivity and associated costs,” they added.

**Antibiotic**

**Antibiotic may improve depressive symptoms in people with low-level inflammation: Study (The Tribune: 20210202)**


Minocycline helped in improving depressive symptoms in patients with treatment-resistant depression with low-grade peripheral inflammation, say researchers

Antibiotic may improve depressive symptoms in people with low-level inflammation: Study

Photo for representational purpose only.

While antibiotics are widely used to treat bacterial infections and other illnesses, a new research suggested that minocycline, an antibiotic with anti-inflammatory properties, improved depressive symptoms in patients with low-grade peripheral inflammation.

The findings of the study were published in the journal 'Neuropsychopharmacology'.

According to the study led by King's College London researchers minocycline helped in improving depressive symptoms in patients with treatment-resistant depression with low-grade peripheral inflammation.

In a four-week randomised clinical MINDEP (Minocycline in Depression) trial, 39 patients with major depressive disorder were recruited from services linked to South London and Maudsley NHS Foundation Trust and via public advertisement.
The trial took place at the NIHR/Wellcome Trust King's Clinical Research Facility at King's College Hospital. The patients, who were taking their routine antidepressant treatment, were split into two groups, one group took daily a placebo (sugar pill) tablet while the other group took daily minocycline alongside their routine treatment for 4 weeks.

Both groups showed similar, significant improvement in depressive symptoms as measured by the Hamilton Depression (HAM-D) Rating Scale. However, patients with higher C-reactive protein (CRP) levels, indicating low-grade inflammation, showed greater improvement in their depressive symptoms when taking minocycline.

Author Dr Valeria Mondelli, Clinical Reader in Psychoneuroimmunology at Institute of Psychiatry, Psychology and Neuroscience, King's College London, and Principal Investigator of the trial said, "Our findings are very exciting because we are showing that patients with increased levels of C reactive protein (an inflammatory biomarker) show good response in terms of reduction of depressive symptoms following treatment with minocycline."

"Of the many patients with depression who do not respond to usual antidepressant treatment, we have shown in previous studies that in at least two-thirds of patients this could be due to the increased levels of inflammation. Now, with this study, we are identifying a potential new effective treatment for these patients," Mondelli added.

Predicting response patients underwent a blood sample to measure biological markers and a clinical assessment at the baseline visit and within 14 days of the trial ending.

Researchers also found that levels of two biological markers, CRP and IL-6, can be used to predict minocycline response in depression. The study identified a specific threshold of CRP levels which is associated with the antidepressant effect of minocycline treatment.

Another inflammatory marker, interferon-gamma, was reduced by the treatment with minocycline but not by placebo, suggesting specific pathways mediating the effects of minocycline on depressive symptoms.

Dr Mondelli said, "We also identified the threshold of CRP levels that is associated with response to this anti-inflammatory treatment. This is very important as we may be able to identify with an easy blood test those patients who are going to benefit from treatment with an anti-inflammatory medication which is already used for other medical conditions and therefore easily available."

Dr Maria Antonietta Nettis, lead author and Clinical Research Associate at Institute of Psychiatry, Psychology and Neuroscience, King's College London, said, "Integrating the measurement of biological markers such as CRP in patients' first assessments could help in identifying potential responders to minocycline, which could be a relatively safe and well-tolerated addition to treatment in immune-related depression."
Although replications in larger samples are needed, the researchers believed that their study has a potentially important clinical impact, as they moved a step towards the identification of personalized treatments for Major depressive disorder (MDD). ANI

**Asthma**

Asthma can be prevented by consuming omega-3 fatty acids *(The Tribune: 20210202)*


1.1 million Children – 1 in 11 – in the UK are currently receiving treatment for asthma

Researchers during a recent study have found that by higher dietary consumption of long chain omega-3 fatty acids during childhood, the risk of developing subsequent asthma reduces in children carrying a common gene variant.

The study, led by the Queen Mary University of London, is in collaboration with the University of Bristol and the University of Southampton, UK, and Karolinska Institutet, Sweden.

In the UK, 1.1 million children (1 in 11) are currently receiving treatment for asthma and most adult asthma begins in childhood. The NHS spends around £1 billion a year treating and caring for people with asthma.

Senior author, Professor Seif Shaheen from the Queen Mary University of London, said: "Asthma is the most common chronic condition in childhood and we currently don't know how to prevent it. It is possible that a poor diet may increase the risk of developing asthma, but until now most studies have taken 'snap-shots', measuring diet and asthma over a short period of time. Instead, we measured diet and then followed up children over many years to see who developed asthma and who didn't."

"Whilst we cannot say for certain that eating more fish will prevent asthma in children, based on our findings, it would nevertheless be sensible for children in the UK to consume more fish, as few currently achieve recommended intake."

Fish is of particular interest because it is a rich source of the long chain omega-3 fatty acids, eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), which have anti-inflammatory properties.

The study, published in the European Respiratory Journal, used data from a large UK birth cohort, children of the 90s, which recruited mothers who were pregnant in the early 1990s and has been following up their offspring ever since. They analysed the association between intake
of EPA and DHA from fish at 7 years of age (estimated by food frequency questionnaires) and incidence of new cases of doctor-diagnosed asthma at 11-14 years of age.

Long chain omega-3 intake from fish was not associated with asthma in the cohort as a whole (4,543 people). However, the team looked in more detail at children with a particular genetic make-up. More than half of the children carried a common variant in the fatty acid desaturase (FADS) gene which is associated with lower levels of long chain omega-3 fatty acids in the blood.

In these children, a higher dietary intake of long chain omega-3 fatty acids was associated with a lower risk of asthma. The risk was 51 per cent lower, comparing those in the top quartile of long chain omega-3 intake with those in the bottom quartile.

Furthermore, this finding was also found in an independent birth cohort study in Sweden (BAMSE).

As they have only found an observational association, the researchers caution that they cannot say for certain that a higher intake of long chain omega-3 fatty acids in childhood can prevent the subsequent development of asthma. The next step is to see if higher intake is also associated with a lower risk of exacerbations in children who already have asthma.

The project was funded by the Rosetrees Trust and The Bloom Foundation. The UK Medical Research Council, Wellcome and the University of Bristol provide core support for Children of the 90s. ANI

**Diseases (Hindustan: 20210202)**

[https://epaper.livemint.com/imageview_612050_53538942_4_1_02-02-2021_6_i_1_sf.html](https://epaper.livemint.com/imageview_612050_53538942_4_1_02-02-2021_6_i_1_sf.html)
आत्मनिर्भर स्वस्थ भारत से बीमारियों का मुकाबला

बजट में स्वास्थ्य सेवाओं के बुनियादी बांधे को मजबूत करने के लिए प्रधानमंत्री आत्मनिर्भर स्वस्थ्य भारत योजना का ऐलान किया है। इसके जरिए बीमारियों की टेक्याम, इलाज और निवारणी सेवाओं को मजबूत बनाया जाएगा। इससे अविश्वसनीय महामारी का सामना करने के लिए स्वास्थ्य तंत्र सक्षम होगा।

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Pandemic

In pandemic age, 137% increase in budget on health, well-being (Hindustan Times: 20210202)

Centre keeps ₹64k cr for Atmanirbhar scheme; allocation for Ayushman Bharat remains unchanged

India’s overall allocation for health and well being has soared by 137% in the financial year 2021-22 to ₹2.23 lakh crore compared to the budgeted spending in 2020-21 as the country seeks to boost the capacity of its health-care system to detect and cure new and emerging diseases in the aftermath of the Covid-19 pandemic.

The Budget unveiled by finance minister Nirmala Sitharaman features a new centrally-sponsored initiative called the PM AtmaNirbhar Swasth Bharat Yojana, with an outlay of about ₹64,180 crores over six years. It set aside ₹35,000 crore for Covid-19 vaccines.

The initiative is aimed at developing capacities of the primary, secondary, and tertiary care health systems, strengthen existing national institutions, and creating new institutions to detect and cure new diseases in the wake of the pandemic that has affected 10.7 million people and claimed more than 154,000 lives in the country. It will be in addition to the National Health Mission.

“…The Budget outlay for health and well being is ₹2,23,846 crores in BE 2021-22 as against this year’s BE of ₹94,452 crores, an increase of 137 percent,” Sitharaman said.

Experts noted that the 137% increase includes many one-time allocations.

“The proposed investment of ₹64,200 crore over six years under the PM AtmaNirbhar Swasth Bharat Yojana is encouraging… excluding Covid vaccinations and water and sanitation expenditure, the remaining healthcare budget has seen a modest increase of 11% (vs. 137% for the overall healthcare budget)…,” said Manoj Garg, director of investments at White Oak Capital, in a statement.

The budgeted expenditure on the Ayushman Bharat health insurance scheme has been kept unchanged at ₹6,400 crore, Garg noted.

“The increase in the healthcare budget from ₹94,500 crore to ₹2.23 lakh crore is driven in large part by budgetary allocations for Covid vaccinations (₹35,000 crore, accounting for 27% of the increase) and an increase in water and sanitation costs (₹74,500 crore, accounting for 58% of the increase),” he added.

This year’s budget proposal rests on six pillars, of which health and well-being is one of the key pillars. The government’s three focus areas in the health segment mentioned by the finance minister were preventive, curative and well-being.
Many inclusions in the budget this year have been made keeping in mind the coronavirus disease (Covid-19) pandemic, and to deal with such public health emergencies in future, that includes setting aside ₹35,000 crore for Covid-19 vaccines, additional grants of ₹13,192 for health, ₹36,022 crore for water and sanitation, and strengthening disease surveillance initiatives by upgrading the National Centre for Disease Control (NCDC).

In order to better the deal with infectious disease outbreaks, the government plans to set up integrated public health labs in all districts and 3,382 block public health units in 11 states, and establishing critical care hospital blocks in 602 districts and 12 central institutions.

The plan for strengthening of the NCDC will also include upgrading its five regional branches, and 20 metropolitan health surveillance units. There will be an expansion of the integrated health information portal to all states and Union territories to connect all public health labs; operationalisation of 17 new public health units and strengthening of 33 existing public health units at points of entry, that is at 32 airports, 11 seaports and seven land crossings.

“The budget provides a much-needed boost to health, nutrition sanitation and pollution control, all of which will contribute to improved health and well being. Primary health care is receiving more support, with even the previously neglected urban component getting new health and wellness centres. The strengthening of disease surveillance system across the country and entry points to the country as well as the laboratory capacity in all districts is also needed for pandemic prevention and epidemic response,” said Dr K Srinath Reddy, founder, Public Health Foundation of India (PHFI).

For enhancing disease surveillance system, the government will also set up 15 health emergency operation centres and two mobile hospitals; along with a national institution for One Health, a regional research platform for the World Health Organisation’s South East Asia Region, and nine Bo-Safety Level (BSL)-3 laboratories and four regional National Institutes for Virology.

“Two or more vaccines are expected soon, and I allot ₹35,000 crore for Covid-19 vaccines in 2021-22, and committed to providing more funds, if required,” Sitharaman said.

The use of another key vaccine, pneumococcal vaccine, that saves children from potentially fatal health conditions such as pneumonia, meningitis, and sepsis will be expanded to other states. Currently, the vaccine is being used only in five states, and will now be rolled out in the entire country.

“It will avoid more than 50,000 child deaths annually in India,” said Sitharaman.

Since malnutrition is one of the primary concerns in India because of which many health-related indicators are still not improving, the government has proposed launching an improvised Mission Poshan 2.0, to strengthen nutritional content, delivery, outreach, and outcomes by merging the supplementary nutrition programme and the earlier Poshan Abhiyan.

An intensified approach is planned to improve nutritional outcomes across 112 aspirational districts.
Covid-19 vaccines

Covid-19 vaccines given a special ₹35k cr allocation (Hindustan Times: 20210202)

https://epaper.hindustantimes.com/Home/ArticleView

The Union government has decided to set aside ₹35,000 crore for coronavirus vaccine in the 2021-22 financial year, finance minister Nirmala Sitharaman said while presenting the Union Budget on Monday, with the promise that more money will be committed if needed.

This is the first time the government has announced monetary commitment at this scale and, back-of-the-envelope calculations showed, it could be enough to buy 1-1.5 billion doses, taking into account rates that India has already been able to negotiate with vaccine makers.

“Two or more vaccines are expected soon, and I allot ₹35,000 crore for Covid-19 vaccines in 2021-22, and [am] committed to providing more funds, if required,” said Sitharaman.

At present, India has two vaccines – Serum Institute of India-manufactured Covishield and Bharat Biotech-made Covaxin. While Covishield has been purchased at around ₹200 per dose, Covaxin costs roughly ₹295 a dose. The amount committed on Monday will buy 1.6 billion doses of the SII-made vaccines and 1.1 billion of Bharat Biotech-made dose. Both need to be taken in two doses, four weeks apart.

“The experiences of the country’s year-long fight with Covid have shaped the Union Budget. This will give a tremendous boost to India’s health infrastructure... The Covid-19 vaccination drive was inaugurated by Prime Minister Narendra Modi ji on 16th January and is presently being given to Health Care Workers and the Frontline Workers; others along the priority pyramid will be given the vaccine in coming times. The Union finance minister has allocated ₹35,000 crore for it and also stated that she will provide more fund if required, which will be a huge boost to the morale of the country,” said the health ministry in a statement.

India aims to vaccinate at least 300 million high risk people in the first phase of Covid-19 vaccination drive, which is expected to last till August. The government has said that for now, it will bear the cost of vaccinating this high-risk population. As on Monday, 3.7 million health care workers were given Covid-19 vaccine doses.


Adar Poonawalla, the CEO of SII, said: “We welcome the FM’s emphasis on healthcare spending, and immunization especially for Covid and the pneumococcal vaccines as this will
help India recover rapidly from this pandemic. This will also encourage expansion in the sector.”

Pregnancy

Study links diabetes during pregnancy with increased risk of heart disease
(Hindustan Times: 20210202)


Study links diabetes during pregnancy with increased risk of heart disease

Women with a history of diabetes during pregnancy (gestational diabetes) are twice as likely by mid-life to develop calcium in heart arteries—a strong predictor of heart disease—even if healthy blood sugar levels were attained many years after pregnancy, according to new research.

The research was published today in the American Heart Association's flagship journal Circulation.

Gestational diabetes, which is high blood sugar levels (glucose intolerance) first recognized during pregnancy, affects approximately 9% of U.S. pregnancies and up to 20% worldwide. After pregnancy, women who had gestational diabetes are at higher risk of developing prediabetes or Type 2 diabetes, conditions that are risk factors for cardiovascular disease.

Previous studies found a much higher risk of heart disease in women with a history of gestational diabetes who later developed Type 2 diabetes. However, it remained unclear whether heart disease risk among women with a history of gestational diabetes was lower for women who attained healthy glucose levels or who developed prediabetes in mid-life.

In 2018, the American College of Cardiology/American Heart Association Cholesterol Clinical Practice Guidelines specified that a history of gestational diabetes enhances women's risk for artery build-up that leads to cardiovascular disease.

Using data from the multicenter, 30-year prospective Coronary Artery Risk Development in Young Adult (CARDIA) study, researchers investigated whether attaining healthy blood sugar levels after pregnancy would mitigate the increased risk of cardiovascular disease that is associated with a history of gestational diabetes.

"CARDIA is the first study to assess heart disease risk in women with a history of gestational diabetes compared to those without gestational diabetes according to their blood sugar levels many years later. Women with previous gestational diabetes had a twofold higher risk of coronary artery calcium if they maintained normal blood sugar levels, later developed prediabetes, or later were diagnosed with Type 2 diabetes many years after pregnancy.
compared to women without previous gestational diabetes who had normal blood sugar levels," said Erica P. Gunderson, PhD, M.S., M.P.H., epidemiologist and senior research scientist in the Cardiovascular and Metabolic Conditions Section at Kaiser Permanente's Division of Research in Oakland, California.

The CARDIA study enrolled more than 5,100 U.S. men and women who were aged 18-30 years at the beginning of the study in 1985. The new analysis includes approximately 1,100 women (49% Black women and 51% white women) without Type 1 or Type 2 diabetes who subsequently gave birth at least once during the 25-year study period, which ended in 2011. Blood tests were performed from before to after pregnancies at five-year intervals to determine if women had normal blood sugar levels, intermediate elevations in blood sugar levels (prediabetes) or they had developed overt Type 2 diabetes. Heart scans were performed to measure coronary artery calcium, a strong predictor for heart disease, at exams 15, 20 and 25 years after the baseline, the first exam of the study.

At the 25-year follow-up, the participants' median age was 48 years old, and 12% of the women in the study had a pregnancy complicated by gestational diabetes. The prospective analysis found

-Women with a history of gestational diabetes had a two-fold higher risk of coronary artery calcification whether they had healthy blood sugar levels, prediabetes or Type 2 diabetes.

-Attaining healthy blood sugar levels after pregnancy did not decrease the risk of developing cardiovascular disease in mid-life for women with previous gestational diabetes.

-Of women with previous gestational diabetes, 36% developed prediabetes and 26% developed Type 2 diabetes, compared to 35% and 9% of women with no history of gestational diabetes.

-25% of women with a history of gestational diabetes had some level of coronary artery calcium vs. 15% of women who never had gestational diabetes.

"We were surprised to discover that women with a history of gestational diabetes are at a significantly greater risk of heart artery calcification, even if they maintain normal blood sugar levels after pregnancy," Gunderson said.

"Our findings represent a shift in this paradigm by showing that normal blood glucose after gestational diabetes is still related to higher coronary artery calcium risk," the authors note.

"Risk assessment for heart disease should not wait until a woman has developed prediabetes or Type 2 diabetes," Gunderson said.

"Diabetes and other health problems that develop during pregnancy serve as early harbingers of future chronic disease risk, particularly heart disease. Health care systems need to integrate the individual's history of gestational diabetes into health records and monitor risk factors for heart disease, as well as the recommended testing for Type 2 diabetes in these women at regular intervals, which is critical to target prevention efforts."
Limitations of the study include that researchers had no measurement of coronary artery calcium levels prior to pregnancy, and coronary artery calcium scores were used as a surrogate marker for heart disease risk not cardiovascular events.

**High omega-3 index**

**Study: Individuals with High omega-3 index are less inclined to die from COVID-19 (Hindustan Times: 20210202)**


Researchers with the Fatty Acid Research Institute (FARI) and collaborators at Cedars-Sinai Medical Center in Los Angeles and in Orange County, CA claimed that people with higher omega-3 index have a lower probability of dying due to COVID-19.

Published the journal 'Prostaglandins, Leukotrienes and Essential Fatty Acids' shows the first direct evidence that higher omega-3 blood levels may reduce the risk for death from COVID-19 infection.

There are several papers in the medical literature hypothesizing that omega-3 fatty acids should have beneficial effects in patients with COVID-19 infection, but up until now, there have been no published peer-reviewed studies supporting that hypothesis.

This study included a hundred patients admitted to the hospital with COVID-19 for whom admission blood samples had been stored. Clinical outcomes for these patients were obtained and blood was analyzed for the Omega-3 Index (O3I, red blood cell membrane EPA+DHA levels) at OmegaQuant Analytics (Sioux Falls, SD). Fourteen of the patients died.

A hundred patients were grouped into four quartiles according to their O3I, with 25 per cent of the patients in each quartile. There was one death in the top quartile (i.e., 1 death out of 25 patients with O3I and gt;5.7 per cent), with 13 deaths in the remaining patients (i.e., 13 deaths out of 75 patients with O3I and lt;5.7 per cent).

In age-and-sex adjusted regression analyses, those in the highest quartile (O3I and gt;5.7 per cent) were 75 per cent less likely to die compared with those in the lower three quartiles (p=0.07). Stated another way, the relative risk for death was about four times higher in those with a lower O3I (and lt;5.7 per cent) compared to those with higher levels.

"While not meeting standard statistical significance thresholds, this pilot study - along with multiple lines of evidence regarding the anti-inflammatory effects of EPA and DHA - strongly suggests that these nutritionally available marine fatty acids may help reduce the risk for adverse outcomes in COVID-19 patients. Larger studies are clearly needed to confirm these preliminary findings," said Arash Asher, MD, the lead author on this study.
Agreeing with Dr. Asher, cardiology researcher and co-developer with Dr. Harris of the Omega-3 Index, Clemens von Schacky, MD, (CEO, Omegametrix GmbH, Martinsried, Germany, and not involved with the study) said, "Asher et al have demonstrated that a low Omega-3 Index might be a powerful predictor for death from COVID-19. Although encouraging, their findings clearly need to be replicated."

Omega-3 expert James H. O'Keefe, Jr., MD, (Director of Preventive Cardiology, Saint Luke's Mid America Heart Institute, Kansas City, MO, and also not involved with the study) observed, "An excessive inflammatory response, referred to as a 'cytokine storm,' is a fundamental mediator of severe COVID-19 illness.

Omega-3 fatty acids (DHA and EPA) have potent anti-inflammatory activities, and this pilot study provides suggestive evidence that these fatty acids may dampen COVID-19's cytokine storm."

The FARI research team is currently seeking funding to expand upon these preliminary observations. Individuals and organizations that want to support this research are encouraged to visit FARI's donations page.

Gene mutations

Panel finds more gene mutations, treatment targets for leukemia (Hindustan Times: 20210202)


A gene panel that looks for about 10 times the number of cancer-causing genes as panels currently used to diagnose and fine tune treatment for a variety of cancers is effective at identifying problematic genes in the most common leukemia, investigators report.

The 523-gene panel, developed by San Diego-based biotech company Illumina, which includes all genes known to potentially cause cancer, can be readily adopted for use in clinical laboratories to diagnose acute myeloid leukemia, or AML, the investigators report in the journal PLOS ONE.

Identifying more genetic mutations in an individual's cancer also enables more targeted treatment for that patient, they say. That includes finding mutations not previously associated with their cancer type, which opens the door to using drugs targeting those mutations that have traditionally been used against other cancers.
"Having a bigger panel gives us more targets," says Dr. Ravindra Kolhe, vice chair for translational research in the Department of Pathology at the Medical College of Georgia at Augusta University.

"Part of what we found here is this 523-panel works for leukemia and that it's a practical and clinically relevant tool for clinical laboratories for routine molecular profiling of blood cancer," said Kolhe, the study's corresponding author.

AML is a distinct disease in every patient because, as investigators are increasingly learning, the gene mutations involved may not be the same in any two patients, says Dr. Vamsi Kota, MCG hematologist/oncologist who directs the Bone Marrow and Stem Cell Transplant Program at the Georgia Cancer Center and AU Health.

"The term 'leukemia' is broad and we should not be treating everyone the same. That is one of the reasons you see the same treatment working for some and not working for others," said Kota, a study coauthor.

The MCG investigators retrospectively analyzed 61 bone marrow samples, which included samples from 40 patients with confirmed leukemia and detailed clinical information on 27 of those patients.

The larger panel identified 880 variants in 292 genes, and only 14.8 percent of the variants were in genes included in the smaller 54-gene panel currently in use by many labs, they write. The remaining 749 variants are not typically assessed in a leukemia diagnosis or detected by the 54-gene panel, they note.

When they looked at the information available on those 749 variants in follow up, they found at least 14 of the variants in 10 genes likely could contribute to AML and 96.2 percent of the patients had at least one of the 14 novel variants. They also found 22 variants in five other genes associated with other tumor types in the vast majority of the patients with AML.

Novel variants identified in the patients might be significant in providing a more complete diagnosis and prognosis for patients and in better identifying treatment that more directly targets their cancer-associated mutations, they say.

There is often overlap in the mutations that contributes to different types of cancer and the broader assessment of mutations present should help identify those.

"The more we know, the more it expands our knowledge of leukemia and expands our ways to treat it," Kota said/

"If you find something abnormal in the genes, which is there in other cancers, then we can use those drugs in these patients," Kolhe added.

"The hope is by finding more of these mutations, we no longer call the cancer by a name but we call it-- and treat it -- by the mutations," said Kota.
The Georgia Esoteric and Molecular Laboratory, which Kolhe directs, was the first in the nation to validate the 523-gene panel by comparing results to established but less comprehensive methods, like polymerase chain reaction used to amplify small segments of DNA to look for suspect changes.

For this study, they also ran the same bone marrow samples multiple times on the 523-gene panel and found essentially 100 percent consistency each time. They also did individual tests looking for specific mutations identified by the panel, and those were consistently on par with the panel's findings as well. They found the larger panel nearly 100 percent effective in clinical sensitivity, specificity, precision and accuracy.

"It's a panel we can consistently do in a lab on a routine basis in a cost-effective way that increases our understanding of the gene mutations contributing to an individual patient's cancer," Kota said.

While noting their sample size was small, there were interesting clinical correlations, like finding seven mutations in a 23-year-old male who had been diagnosed with two mutations.

The new mutations they found included two novel variants now associated with leukemia and other cancers, they say. The patient, who had the highest number of gene mutations identified by the larger panel, only survived four months and two days.

Kota notes that decades have passed without any real advancements in AML treatment, but this year six new drugs, which target six mutations identified by the smaller gene panels, have been approved. Kolhe hopes the new panel will help expand that new drug number at least 10 times as well.

"The idea of having a bigger panel is not only confirming what we already know about which mutations are associated with a cancer but identifying new ones," Kolhe said.

"What we are doing is taking that 50-gene panel and going to the next level with a 523-gene panel and one of our goals includes identifying 60 new targets within the next five years," Kolhe said.

Most patients with AML relapse within three years of diagnosis, and broader identification of treatment targets should improve those percentages, they say.

The National Comprehensive Cancer Network recommends that testing for AML include molecular analysis for at least those six genes now known to be causative for AML.

Current guidelines also suggest the use of the multi-gene panels and next-generation sequencing for a comprehensive prognostic assessment. Next generation sequencing is a high-throughput approach, like the 523-gene panel, that enables investigators to efficiently sequence a large number of genes at one time, even the entire genome in a day's time. Sequencing means looking at the order of the four base pairs of DNA -- A, T, C and G -- to find changes that cause disease.
Kota and Kolhe say that while the smaller gene panels are cost and time efficient, they provide an incomplete mutational profile, including omissions of several known hotspot mutations. The increased understanding of the molecular heterogeneity of blood cancer, and other cancers as well, make the broader assessment logical, they say. They note that the cost of the broader panel is no higher than testing for the six AML-associated genes.

Blood stem cells from the bone marrow produce both white blood cells that help us fight infection and blood-forming cells called myeloid cells, and AML may affect both.