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Editorial Board

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Editorial

Pandemic to Pan-endemic: Story of Covid-19

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The World Health Organisation [WHO] declared Covid-19 as a pandemic on 11 Mar 2020.[1] The world was gripped in the clutches of an illness, hitherto, seen in only in few regions of the world like Severe Acute Respiratory Syndrome [SARS] & Middle East Respiratory Syndrome [MERS] caused by SARS-COV and MERS-COV, respectively.[2] This one created enough havoc to overwhelm the healthcare infrastructure all over the world. There was universal concern almost bordering on fear & uncertainty. The words like 'isolation', 'quarantine', 'lockdown' and 'RTPCR' were probably the most spoken words across all regions of the world. Region by region, the illness eventually showed what it was capable of. There was hardly any region of the world by end of 2020, which had not witnessed the wrath of COVID-19.

It is difficult to enumerate the multitude organizations and industries which had to bear the brunt of the illness. The governments and political leaders had to take the tough decisions of lockdowns and travel restrictions. They were also involved in chalking out the ways to get the citizens of their respective countries all over the world back to homeland. The ministries of health as well as the leaders of healthcare institutions were on constant war footing with respect to the medical guidelines for testing, quarantine, isolation, and treatment of patients. At the hospital and clinics, the challenges were numerous- separating covid related wards from routine wards and OPDs, provision of adequate PPEs, oxygen, and beds with ventilators to maintaining adequate staff and motivating them for round the clock duties beyond the routine call of duty. There were herculean efforts towards equipping the existing hospitals with adequate beds, oxygen and ventilators as well creating crisis expansion set-ups in form of make-shift dedicated covid hospitals and isolation centers. Despite these endeavors, there was always a shortage of beds during the various waves at different time points world over. The rich and the developed nations too felt the stretch on the healthcare facilities. This led to upscaling of the infrastructure thereby being prepared for the next wave. In India, the third wave witnessed better preparation as well as handling of the surge in the cases.

The maintenance of supply chain lines was a challenge at multiple levels. The common man on the street had his own challenges. The task of maintaining the home supplies during lockdown, jobs security and layoffs, effect of the illness and lockdowns on the mental state etc were contests which the common man had to endear . The covid appropriate behavior was tough to accept and institute at the onset of the pandemic and required policing as well as fines for violating the same. There were limitations on the number of people at gatherings like religious, marriages or funerals. This was tough to abide by but was adhered to at most places.

The surge in the research in myriad fields related to COVID-19 is evident by the spike in numbers of scientific articles related to COVID-19 starting Jan 2020. The vaccine research has broken all records. The funding, production, distribution as well as administration has been a success story so far. Rapid vaccination drives and alteration of the schedule on post marketing serological surveys led to optimization of the doses for a larger population. At the time of writing of this manuscript, India has two states with 100% vaccination of both doses for all the population and most of the states bosting of more than 90% for two doses. This has led to a sense of safety and has led to opening of travel restrictions as well as increased movement of people. The opening up of offices, schools and colleges, markets and public places has led to resumption of the traffic and density of people on the roads as well as closed areas. There has been no adherence to social distancing and there is a drop in the covid appropriate behavior with many shunning the masks and

hand hygiene. The third wave of this country has been much milder than the second wave in April-May 2021. This has further fueled the thoughts of complacence of covid appropriate safety measures. The data of the cases and serological surveys periodically conducted provide proof that endemicity of COVID-19 increased 3-fold between first and second waves.[3,4,5] The third wave has seen much more infections due to the transmissibility of the omicron variant and this has surely increased the seroprevalence further.

This period of two years since Feb 2020 has seen shades of change in human behavior. From fear and unimaginable fads at the onset of the pandemic, people and societies have currently accepted this illness as one akin to routine flu. Understanding of the mechanisms and pathophysiology of the disease, availability of extensive data on the behavior of the virus and its effect, recovery from active infection providing natural immunity and the extensive and successful vaccination drive have given confidence to return to pre-COVID era. However, there are still uncertainties which exist. Will the virus mutate further to another severe disease-causing strain? Will there be another wave which will once again test the tenacity of the preparedness so far? Will the natural immunity or vaccination last long enough? What will be the long-term effects of the infection? Was this a natural zoonotic infection or a man-made disaster? From pandemic to endemic, the disease has followed the course of the previous pandemics. The future is still unsure but there is hope and definitely, better preparedness unlike earlier pandemics.

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Letter to the Editor

The Infirmities of Indolence

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The World Health Organization (WHO) defines physical activity as 'any bodily movement produced by skeletal muscles that require energy expenditure'.[1] Apart from the long list of conditioned activities that the definition brings to one's mind, physical activity is anything that involves moving from one place to another to fulfil a task or to achieve a goal. It should not be confused with 'exercise' or 'physical fitness', which are activities that one performs to enhance their physical attributes like endurance, muscle strength, stature or appearance.

Unlike other animals, the body of humans has evolved to carry out skilled activities to complement their higher intellectual ability; however, the clear anatomical and physiological distinction between upper and lower limbs is a reminder that evolution did not sacrifice motility for dexterity. Physical activity is essential for survival and contributes greatly to quality of life. Physical activity can also be viewed as a preventive measure for the complications that one can develop following long periods of physical inactivity.

A large-scale study which collected data from 1.9 million participants, shows that the global prevalence of insufficient physical activity was 27.5% in 2016.[2] The prevalence has been stable since 2001 with previous estimates showing a global prevalence of 23.3% in 2010. However, this problem is not limited to adults more than 18 years of age. The Global Health Observatory Data shows that nearly 80% adolescents (aged 11-17 years) did not meet their daily requirements of physical activity.[3] In both these studies, a greater proportion of females were found to be less active as compared to males.

These numbers just highlight the tip of the iceberg. The pressing issue of physical inactivity is being ignored by the masses and has a great implication on the health of the community as a whole. Insufficient physical activity, unlike infectious diseases, does not manifest acutely or sub-acutely, instead plays a major role in disease progression of chronic lifestyle diseases.

A study in 2012 [4], summarised that prolonged periods of insufficient physical activity can lead to maladaptation in the human body, leading to a substantial decrease in the number as well as the quality of years of life. It highlighted conclusive evidence to prove that physical inactivity is an important preventable cause and/or risk factor of most chronic diseases such as metabolic syndrome, obesity, insulin resistance, pre-diabetes, type 2 diabetes mellitus

(DM), gestational diabetes, preeclampsia, polycystic ovary syndrome (PCOS), and even cognitive dysfunction, depression, and anxiety.

Insufficient physical activity is indicated in the pathophysiology of endothelial dysfunction and dyslipidemia, thereby increasing the risk of cardiovascular diseases such as coronary artery disease (CAD), peripheral artery disease, hypertension, stroke, congestive heart failure (CHF), and deep vein thrombosis (DVT). If prolonged, it can result in osteoporosis, osteoarthritis, imbalance/falls, pathological fractures, rheumatoid arthritis, erectile dysfunction, diverticulitis, constipation, non-alcoholic fatty liver disease and gallbladder diseases.

Physical inactivity can help prevent or delay the progression of cancers such as colon cancer, breast cancer

and endometrial cancer. Eventually, insufficient physical inactivity can accelerate the biological age of the human body and may even cause premature death.

Conclusion

Medical evidence has been able to show a strong association of physical inactivity with chronic diseases, a few of which have been mentioned in this article. However, the aim of this article is to address the 'elephant in the room', which is, that 1 in 4 people across the globe are physically inactive. It is the need of the hour to realise the importance of physical activity in our daily lives, or else fall into the vicious cycle of consequences that leave an ill impact on the health of the individual, as well as the community.

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Original Article

YouTube as a source of information on basic measures to prevent COVID-19: A cross-sectional study

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ABSTRACT

Introduction: The COVID-19 pandemic is the largest public health emergency of the century and its successful management depends on the effective dissemination of factual information. YouTube is the second most visited website and the second largest search engine in the world. However, it has no policy of filtering videos; for this reason, there are many videos online, and while some may be useful, others may be misleading. The objective of the study was to evaluate this platform as a source of information on basic measures to prevent COVID-19.

Methodology: A YouTube search was conducted using keywords 'COVID-19 prevention' and 'Corona prevention'. First 60 videos of each search term were included and analysed to check whether they provided information on the seven basic measures to prevent COVID-19 in accordance with the WHO. Each video was given an overall rating of 0-7. Source of videos, total views, number of days since upload were noted.

Results: Of the 120 videos, 33 videos were selected for study. Mean content score and views per day of all videos assessed were 3.91 and 1502.51 respectively. Of these, 18 videos were uploaded by health organizations, healthcare institutes and hospitals. Mean content score and views per day of these videos were 4.33 and 2266.71 respectively. 15 videos were uploaded by other sources. Mean content score and view per day of these videos were 3.27 and 585.5 respectively. There was a statistically significant difference in content score and views per day among videos based on source.

Conclusion: Majority of videos in English on YouTube on the study day were not complying with the WHO guidelines in terms of providing basic information to

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prevent COVID-19. Health related organizations and other knowledge holders should be more involved in the production of videos to provide accurate information on this subject to the general public.

Introduction

The World Health Organization (WHO) on March 11, 2020 declared the current outbreak of coronavirus disease (COVID-19) a pandemic.[1] It is evolving every day and imperilled life worldwide across social and economic front.

The principal way the infection spreads is by respiratory droplets among individuals who are in close contact. The other mode of transmission is by touching the contaminated surfaces, then touching their nose, eyes or mouth.[2] Accurate information and guidance about personal behavior is, therefore, one of the most important elements in limiting the spread of COVID-19.

Recent advances in information technology have made the Internet an attractive resource for health-related information searches by healthcare providers and the public.[3] YouTube is the second most visited website and the second largest search engine in the world.[4] More than 2 billion users visit YouTube every month, and people watch more than 1 billion hours of videos, which are viewed billions of times.[5]

Not only the general public or patients, but also medical institutions and professionals use and exchange information through YouTube. While YouTube is a great educational tool that healthcare professionals can use to spread information and influence public behavior, it can be a source of misleading information if not used correctly.

In connection with the COVID-19 pandemic, the outbreak of infodemic has escalated to a level that requires planned action. Infodemics are excess information that occur during a pandemic, some of which are accurate and some of which are not. It makes it difficult for individuals to get reliable guidance when they need it. False information spreads more and more rapidly, making it difficult to respond to health emergencies.[6] Infodemiological research is increasingly needed because it can provide important insights into the health-related systems of the population. Infodemiology is a survey of distribution and information determinants on the Internet or in the general public, with the aim of providing information to public health and public policy.[7]

Content analysis of YouTube videos provides public health professional with the overview of the information that the population is most likely to receive. Several studies have investigated the content of YouTube videos in previous pandemics, such as the H1N1 pandemic, Ebola outbreak, and Zika outbreak. [8-10] These studies found that a significant number of YouTube videos were misleading. Similar studies were conducted within two months after the WHO's classification of COVID-19 outbreak as a pandemic, found that most of the video content was inappropriate and suggested few guidelines for dissemination of accurate medical information to the general public on YouTube.[11-15]

YouTube search results are dynamic, and will change when new videos are uploaded or old videos are removed. So, it will be interesting to see the contents of YouTube videos after six months of the declaration of a pandemic. The objective of this study was to evaluate the content accuracy of the YouTube videos that provide information in English on the basic measures to prevent COVID-19 according to WHO guidelines**.**

Methodology

On September 29, 2020, a YouTube search was conducted using the keywords 'COVID-19 prevention' and 'Corona prevention'. The only search filter used was 'sort by relevance' as the default filter for YouTube searches. Videos were searched after clearing of cache and using a new YouTube account to minimize results biased by cookies, personal settings, and browser history. More than 90% of YouTube users clicked only the first 3 pages (i.e., 20 videos x 3 pages = 60 videos) of search results to receive the desired information.[10] However, YouTube no longer uses pages to display results, and instead displays them in the form of a continuous list. Therefore, the first 60 videos for each search term were included in this study.

Duplicate videos, which were not in English, more than 15 minutes in length, and not related to COVID-19 prevention, were excluded. Uniform resource locators for all video samples included in the study have been saved for data archiving and future reference. Included videos were analyzed to check whether they provided information

on the seven basic measures to prevent COVID-19 in accordance with the WHO[16] (Table 1).

Table 1: Content score in accord with WHO guidelines

Basic measures to prevent COVID-19	Score
Wash your hands regularly with soap and water, or clean them with alcohol-based hand rub	1
Maintain at least 1 metre distance between you and the people that are coughing or sneezing	1
Avoid touching your face	1
Cover your mouth and nose when coughing or sneezing	1
Stay home if you feel unwell	1
Refrain from smoking and other activities that weaken the lungs	1
Practice physical distancing by avoiding unnecessary travel and staying away from large groups of people	1
Total	**7**

Each measure was given a score as 0 (not available) or 1 (sufficient information), and each video was given an overall rating of 0-7. The total views, number of days since upload were recorded. The number of views per day was calculated as the total number of views divided by the number of days since the upload.

A Google search was performed for each YouTube ID to find the upload source. The videos were grouped into:

Group 1- uploaded by health organizations, healthcare institutes and hospitals.

Group 2- uploaded by other sources.

All videos were reviewed and analyzed by two independent researchers. Disagreements among the researchers regarding the scoring criteria of a particular video were resolved by discussing the issue until a consensus was reached.

Statistical analysis was performed using the IBM SPSS 20 statistical software (IBM, Armonk, NY, USA). Mean, standard deviation was calculated for all the variables. Independent *t*-tests were done to compare the mean values. A *p*- value <0.05 was considered significant.

Results

Of 120 videos, 87 were excluded from the study because they were repeated (n=29), not in English (n=16), did not address the primary topic (n=36), duplicate footage (n= 2) and exceeding 15 min duration (n= 4) and 33 videos were selected for study and evaluated. The descriptive statistics of the evaluated videos are shown in Table 2.

Table 2: Descriptive statistics of evaluated videos

Variable	Minimum	Maximum	Mean	Standard deviation
Views per day	2.58	21719.48	1502.51	3946.20
Content score	1	6	3.91	1.40

Out of 33, 18 videos (54.5%) were uploaded by health organizations, healthcare institutes and hospitals, while 15 videos (45.5%) were uploaded by other sources. Analysis of videos with respect to the sources of upload is shown in Table 3.

There was a statistically significant difference in content score and views per day among videos based on source.

Regarding individual basic measures for preventing transmission of COVID-19, none of the videos evaluated in this study warn viewers to refrain from smoking and other activities that weaken the lungs. All videos included in this study discussed about the hand hygiene measures. Percentage of videos that addressed basic measures to prevent COVID-19 is shown in Table 4.

Table 4: Percentage of videos that addressed basic measures to prevent COVID-19.

Basic measures to prevent COVID-19	Percentage (No. of Videos)
Wash your hands regularly with soap and water, or clean them with alcohol-based hand rub	100% (33)
Maintain at least 1 metre distance between you and the people that are coughing or sneezing	63.6% (21)
Avoid touching your face	69.7% (23)
Cover your mouth and nose when coughing or sneezing	69.7% (23)
Stay home if you feel unwell	54.5% (18)
Refrain from smoking and other activities that weaken the lungs	0
Practice physical distancing by avoiding unnecessary travel and staying away from large groups of people	27.3% (9)

Table 3: Descriptive statistics of evaluated videos with respect to sources of upload

Variable	Group 1				Group 2				*P* Value
	Minimum	Maximum	Mean	Standard deviation	Minimum	Maximum	Mean	Standard deviation	
Views per day	3.21	21719.48	2266.71	5120.30	2.58	5529.44	585.50	1451.51	0.0001*
Content score	2	6	4.33	1.24	1	5	3.27	1.33	0.0244*

Discussion

Knowledge about pathology, and the epidemiology of COVID-19 is rapidly developing. What we know at this time is that personal action is the best way to prevent COVID-19 infection. YouTube is becoming more accessible and viewed for health information by the general population. Healthcare providers in all disciplines and fields of medicine must understand how people can access limited or misleading sources of information. The objective of this study was to evaluate the accuracy of the content of YouTube videos that provide information in English on the basic measures to prevent COVID-19.

Of the 120 videos, 87 were not included because they did not meet the inclusion criteria. Like previous studies, we found

that the high exclusion rates made it difficult to find the necessary content on YouTube.[17-20] Despite the enormous amount of information available on the Internet, the unstructured formats often make it difficult to obtain the required information.

The average content score of the videos uploaded by health organizations, healthcare institutes and hospitals was significantly higher than that of videos uploaded by other sources. The most frequently reported basic preventive measure was hand hygiene while none of the videos evaluated in this study informed viewers to refrain from smoking and other activities that weaken the lungs. The harms of tobacco use are well established. Tobacco causes more than 8 million deaths each year from cardiovascular diseases, lung disorders, cancers, diabetes, and hypertension.[21] Tobacco smoking is also a known risk factor for severe disease and death from multiple respiratory infections.[22]

The result of some non-peer reviewed preprint articles falsely suggesting smokers are less likely to catch coronavirus have led to headlines saying that smokers are protected against COVID-19.[23] This led to the WHO releasing a statement on May 11, 2020 urging caution with regards to these claims, and emphasizing the lack of evidence confirming a link between smoking or nicotine in the prevention or treatment of COVID-19.[24] On Jun 30, 2020, WHO recommended tobacco users to stop using tobacco, which was based on a review that included thirty four peer reviewed studies on the association between smoking and COVID-19, suggests that smoking is associated with increased severity of disease and death in hospitalized COVID-19 patients.[25]

In addition to the classic tobacco smoking behavior, the use of water pipes and electronic cigarette use should not be overlooked. These modes of consumption can increase the contamination risk due to repeated hand-to-mouth interactions, carrying cigarette packs in the pockets, and blowing of smoke. Similarly, exposure to passive smoke can alter the expression of ACE- 2 gene and can cause changes in the immune system. Naturally, these patients can also exhibit severe COVID-19 symptoms, and smoke exposure is a potential risk factor for those around them, including their friends and family.[26]

Accurate information and guidance on personal behavior is one of the most important elements in stopping the spread of COVID-19. There are two components of preventing the disease: reducing exposure and reducing susceptibility. Basic measures to prevent transmission of COVID-19 can be difficult to understand, especially for a significant segment of the public with poor literacy skills. The video presentation is a potentially useful alternative for conveying important information to the public. This study demonstrated that the information on the basic measures for preventing transmission of COVID-19 on YouTube is unsatisfactory, which we believe represents an important missed opportunity for disease prevention.

The study found that the included videos were viewed over 1500 times a day, reflecting YouTube's considerable reach as a way of communicating with the public. Videos uploaded by health organizations, healthcare institutes and hospitals had significantly more views than those uploaded by individuals without medical credentials which suggests a greater level of trust by the public in these healthcare organizations. Official associations should take greater responsibility for the

dissemination of accurate and complete health related information on the Internet.

We have learned a lot from this COVID-19 experience. While it might take some time for a vaccine to become available, a second wave of COVID-19 surge, despite the fact that it is not definite, might hit us anytime.[27] We should not use this time to celebrate, but to plan. In the best traditions of emergency preparedness, we should hope for the best, but plan for the worst.[28] YouTube may be a significant resource for dissemination of information about COVID-19 and should be targeted by healthcare agencies for this use. This may play a significant role in successfully managing the COVID-19 pandemic.

The limitation of the current study was that the search results are dynamic and will change when new videos are uploaded or old videos are removed. This cross-sectional study showed information at that time. It is likely that the outbreak of COVID-19 will continue to grow and the content presented on YouTube will most likely shift and evolve. The videos available on YouTube are constantly changing due to the search algorithm. It should also be noted that different videos can be accessed with different key words. Lastly, all videos included were in the English language only.

Despite these limitations, we believe that important details and information can be obtained from this study for the accurate and complete delivery of medical content through online platforms.

Conclusion

This study shows that the information on YouTube videos in English about basic measures to prevent COVID-19 according to the WHO was incomplete. We missed an important opportunity to prevent transmission of disease. The medical fraternity should take note of the tremendous reach of YouTube and, should consider using influential online broadcasting platforms for the dissemination of accurate medical information to the general public.

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Original Article

A study on knowledge, awareness, and outlook on Nanorobotics in Cancer treatment among undergraduate medical students in Telangana.

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ABSTRACT

Introduction: Cancer is the second leading cause of death globally. Statistics reveal that an estimated 9.6 million deaths have occurred worldwide in 2018 (WHO). Nanorobotics is an emerging field of nanotechnology which deals with design and construction of devices at nanoscale (10^{-9}). Nanorobotics is rapidly progressing and is being implemented to solve several limitations of conventional cancer treatments such as non-specific bio distribution and targeting, lack of water solubility, poor oral bioavailability, and low therapeutic indices. The multifunctional nanorobots are now being actively investigated and are on the horizon as the next generation of nanoparticles, facilitating personalised and tailored cancer treatment.

Methodology: An observational type of cross-sectional descriptive study was carried out among 450 undergraduate medical students in Telangana. A structured questionnaire was given to assess the knowledge, awareness, attitude and willingness of nanotechnology in cancer treatment. The results thus obtained were analysed.

Results: Majority of the students were curious to know about the use of nanorobotics in cancer treatment. Even though more than half of them already knew about nanotechnology, very few had knowledge about its use in medicine. Around 78% chose nanotechnology over conventional methods of cancer treatment. Many thought high production cost as a major drawback in bringing nanotechnology into India and suggested active research as the best possible solution.

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Conclusion: Nanorobotics can serve as a potential cancer treatment, which is safer than present treatment modalities and specific as well. This study clearly shows the lack of knowledge among medical students about the usage of nanorobotics in medicine. Therefore, there is a need to increase awareness of nanomedicine through informative posters, convenient administrative and documentation processes. This study has shown positive attitude of students towards nanotechnology. Possible drawbacks and approaches to overcome them are discussed in this study.

Introduction

Cancer is a large group of diseases that can start in almost any organ or tissue of the body when abnormal cells grow uncontrollably. It is the second leading cause of death globally after cardiovascular disease.[1]

Statistics reveal that an estimated 9.6 million deaths have occurred worldwide in 2018 (WHO)[2] and more than 1300 people die of cancer every day in India (ICMR - 2017). Though 60% of cancers can be avoided by simple behavioural changes, they require technological innovation to improve outcomes.[3]

Classical cancer therapies that are still clinically used include chemotherapy, radiotherapy, and surgery. The main drawbacks of these therapies are their lack of specificity—apart from affecting cancerous cells, it also damages the surrounding cells/tissue, development of multidrug resistance during treatment, and the limitations can go as far as recurrence.[4]

Though radiotherapy has been proven efficient in dealing with cancers that are localized in specific body sites, even it carries several disadvantages varying from recurrence to morbidity to induced cancers.[5] Therefore, looking for newer techniques is vital.

Among several emerging technologies over the past two decades (e.g. immunotherapy, cell therapy, gene editing etc.), application of nanotechnology in treatment and research of cancer has surged and gained great attention due to their multifunctionality and improvement on cancer therapy. Nanotechnology offers many possible benefits to cancer therapy, detection, and diagnosis such as combination therapy, tumour targeting, controlled release, long circulation, reduced toxicity, and concurrent live imaging.

Cancer nanorobotics solves several limitations of conventional cancer treatments such as non-specific biodistribution and targeting, lack of water solubility, poor oral bioavailability, toxicity, and low therapeutic indices. The mechanisms of action of these nanorobots are like-

Targeted drug delivery:

Nanoparticles (NPs) possess unique properties such as their small size, ability to load various drugs, large surface area and ability to increase the absorption of conjugated drugs. Therefore, the NPs have been considered as excellent tumour-targeting vehicles.

Tumour Targeted therapy:

The basic advantage of nanoparticles is their ability to differentiate malignant from non-malignant cells and selectively attack tumour cells. Two fundamental processes are involved in this process: passive and active targeting.

Passive targeting takes advantage of the Enhanced Permeability and Retention (EPR) effect to increase the concentration of nanoparticles (NPs) in the tumour.[6]

Various drugs and biomolecules like monoclonal antibodies and nucleic acid aptamers are conjugated with nanoparticles to direct them to specific target receptors on malignant cells. Active targeting enhances drug/NPs accumulation, intracellular uptake, and penetration of physiological barriers which block drug access to some tumours.[7]

Hyperthermia:

Hyperthermia therapy (HTT) is applied with magnetic nanoparticles (MNPs) under radiofrequency magnetic field to selectively increase temperature at the tumour site.[8]

DNA thrombin model (aptamer):

An autonomous DNA robot constructed using DNA origami is programmed to transport payloads and present them specifically in tumours. The intravenously injected DNA nanorobots deliver thrombin specifically to tumour-associated blood vessels and induce intravascular thrombosis, resulting in tumour necrosis.[9]

Quantum dots:

Quantum dots represent a superior class of fluorescent nanoprobes for optical imaging with tuneable properties, high stability, and the ability to target tumours with accuracy and in sentinel lymph node mapping based on surface

functionalization.[10] Nanorobots can be used in other diseases like atherosclerosis, diabetes, kidney stones etc. and processes like gene therapy and surgery.[11] Multifunctional and multiplex nanorobots are now being actively investigated and are on the horizon as the next generation of nanoparticles, facilitating personalised and tailored cancer treatment. The utility of nanotechnology can provide a "revolutionary", rather than "evolutionary" improvement in cancer treatment. The aim of this study is to assess the knowledge, attitude, and willingness of **Nanorobotics in cancer treatment** among undergraduate medical students in Telangana.

Methodology

An observational type of cross-sectional descriptive study was conducted among undergraduate medical students in registered medical colleges in Telangana. Sample size was calculated using $4pq/l^2$; where p=61.2, q=38.8, l=7.5% of 61.2=4.59. Sample size = $4pq/l^2 = 4* 61.2 *38.8/ 4.59^2 = 450$. Undergraduate MBBS students were included in the study. Students studying in other courses and those who didn't consent were excluded. Students were explained about the research and its importance. A structured questionnaire was distributed and results were analysed using Microsoft Excel and SPSS (Statistical Package for Social Sciences version 25.0 software).

Results

The sample size was calculated as a minimum of 450 by calculating proportion as 61.2% from the pilot study and assuming 7.5% error and 10% non-response rate. We visited various medical colleges in Telangana. Every student in a registered medical college of the state was eligible for the study. Each student was examined for eligibility.

Number of potentially eligble candidates =500+

Number of candidates examined for eligibility=500+

Number of candidates confirmed eligible =450

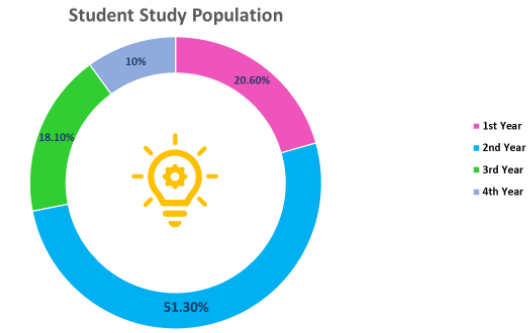
Number of candidates included in study=450

Number candidates who filled the questionnaire=450

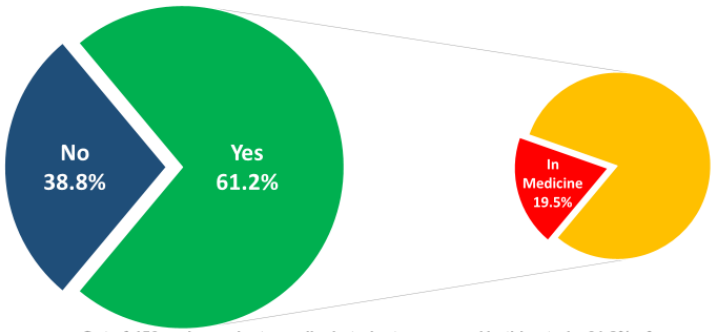
Number of responses analysed =450

Candidates who were not willing to participate were excluded

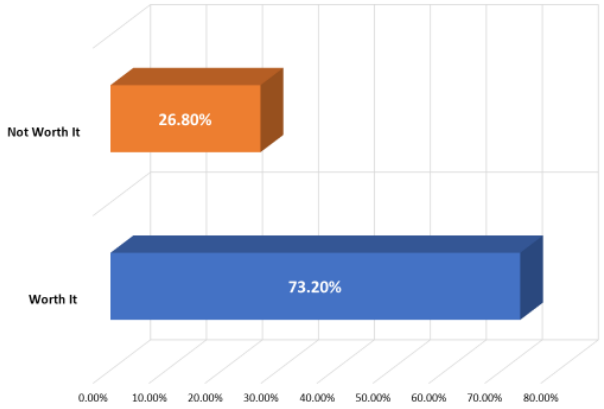
Students who were not willing to participate were excluded from the study. The total number of candidates with confirmed eligibility were 450. The total number of responses analysed was 450 (follow flow chart).



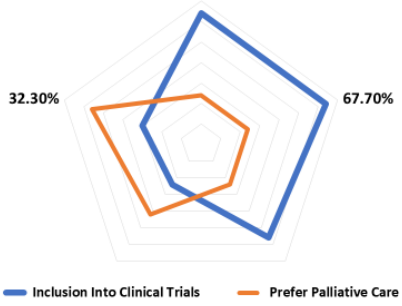
Undergraduate medical students were included in the study.



Out of 450 undergraduate medical students assessed in this study, 61.2% of students were aware of term "Nanotechnology" whereas its application in medicine was known only among 19.5% of students.

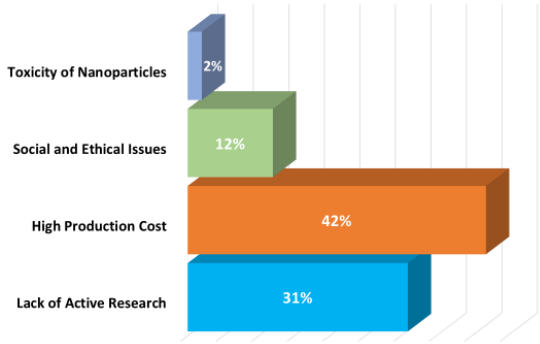


Nanotechnology in India still has just begun to take shape in India. Ensuring availability and using to its fullest capacity would require a lot efforts in terms of economy, manpower and most importantly, time. Majority of students think that it is worth to devote resources into it.

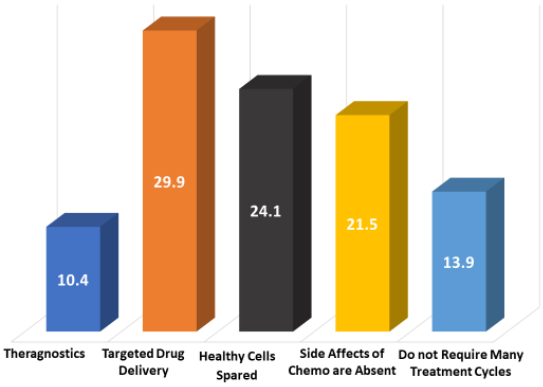


A hypothetical situation of terminal staged cancer patient consulting them was given and asked for their next step in treatment. Inclusion of patients into clinical trials as a last resort was preferred before resorting to palliative care which shows positive attitude of students towards nanotechnology.

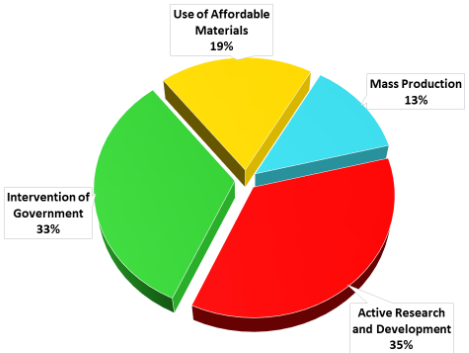
Similar to any other technology, Nanomedicine is associated with its own drawbacks. Greater part of students (67.5%) think that its positive effects will overweigh the negative ones.



Considering obstacles in progress of nanotechnology in India, students inclined towards high production cost as a potential drawback over lack of research, social and ethical issues and toxicity of nanoparticles.

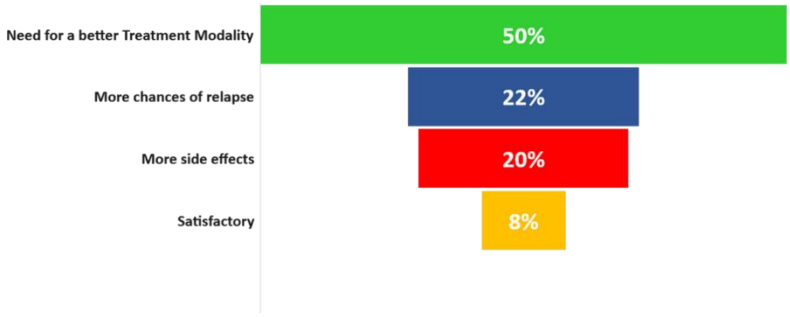


When asked about the advantages of nanotechnology in the treatment of cancer, targeted drug delivery was opted the most followed by other advantages of nanomedicine.



When opinions were asked on strategies to make nanotechnology cost effective, Utmost preference has been given to Active research and Development.

Opinion regarding present treatment options were asked and 20% of students were concerned regarding numerous side effects of present treatments and 22% with increased chances of relapse. Only 8% were satisfied with present methods.



Discussion

Every invention and technological innovation is received with an air of scepticism. While some are fast to pick sides and voice their support, there are those who hold back to watch where this new chapter would lead. Caution is necessary whereas bias will only serve as a roadblock. Pursuing nanotechnology as a research initiative and a potential therapeutic option, it is important to note that any outcome is possible and an open mind will safeguard us against prejudice. Beginning its journey in the '80s, Nanotechnology has made remarkable advances over decades, with its commercial application beginning in the '00s with the introduction of liposomes, quantum dots and micelles.[11] As we move towards a new era, the flexibility of both mind and body to adapt to new outcomes will make future clinicians and surgeons more prepared for what they will have to face in their practice of treating a variety of patients.

Nanotechnology has intrigued the science community and made the world hope for a brighter future with its increased specificity in targeting tissue, large surface area and a wide range of operations that can be conducted at a nano level. Nanotechnology also opens a new realm of reactions in the nano level which cannot be mimicked by the conventional drugs. In cancer treatment specifically, they aid in early detection, and rapid diagnosis of malignancies, which is a crucial determinant to treatment and prognosis. In a study by Shi et al[12], light has been shed on the mechanism by which Nanorobots have access to the Tumour Micro Environment (TME) by what is termed as Enhanced Permeability and Retention effect (EPR) which helps in site specific interactions, thus saving the adjoining tissue from damage.

In a review stated by Ferrari et al[14], he talks about the theranostic and multi-pronged approach of nanoparticles called Nanovectors which not only aid in specific delivery of therapeutic agents but also imaging of the cancer molecular environment with the help of target markers. Nanotechnology is being developed to aid in both in-vivo and ex-vivo detection of markers through a non-invasive method.An observational study was conducted in a population of 450 undergraduate medical students in the region of Telangana, by use of an ethically approved questionnaire with the overview of assessing the knowledge, awareness, and willingness of students towards Nanotechnology and its applications in cancer treatment.

A total of 61.2 % of students were aware of Nanotechnology but only 19.5% of students were aware of its use in the medical field. When students were educated on the different mechanisms and modules that were developed thus far till 2019, 42 % seemed to blame high production costs as one of the major hindrances. 35% thought active research and development would factor high in propelling advances further and making it cost effective.

High productive cost was stated as one of the causes holding nanotechnology back in a review written by Zhang et al.[14] As the difference in size, shape and material used for the make of every nanorobot might vary, simplifying the process might prove effective in making nanorobots more cost-effective.

In our study, 78.1 % of students insisted on focusing the prowess of nanotechnology in diagnostics and therapeutics of cancer. On a more ethically thought-provoking note, 67.7% of students inclined towards the possibility of including patients in active trials as a last resort before moving on to best supportive care.

In assessing the knowledge of fellow undergraduate students through our study, we aim to direct the attention to the backstage and unseen crowd of the next generation. As important as it is to keep ourselves up to date with daily news, we believe it is equally important to educate ourselves and our fellows on every step that is taken to aim for better healthcare. It would also inform and serve as a source to understand how a certain innovation would be accepted into the medical fraternity and its impact.
In our study, there was no bias in choosing the study population and were asked to fill the questionnaire after giving their consent. As most of the study population was of a younger age group ranging from first to final year medical students, the data collected could show a shift towards

lesser awareness and different opinions of a less clinically aware group.

Conclusion

This study has revealed less knowledge of nanomedicine among undergraduate medical students. Potential drawbacks like production cost, toxicity and approaches to deal with them (use of affordable materials, active research and development) are discussed in this study. Overall, students are inclined towards dedication of resources for making nanomedicine ubiquitousEvery invention and technological innovation is received with an air of scepticism. While some are fast to pick sides and voice their support, there are those who hold back to watch where this new chapter would lead. Caution is necessary whereas bias will only serve as a roadblock. Pursuing nanotechnology as a research initiative and a potential therapeutic option, it is important to note that any outcome is possible and an open mind will safeguard us against prejudice. Beginning its journey in the '80s, Nanotechnology has made remarkable advances over decades, with its commercial application beginning in the '00s with the introduction of liposomes, quantum dots and micelles.[11] As we move towards a new era, the flexibility of both mind and body to adapt to new outcomes will make future clinicians and surgeons more prepared for what they will have to face in their practice of treating a variety of patients.

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Original Article

Study on Knowledge, Attitude and Practice of Consanguineous marriages among medical and non-medical students

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ABSTRACT

Introduction : Consanguineous marriages (union between two individuals sharing common ancestor) in varying degrees is a deeply rooted social and cultural trend in most parts of India and other countries. This has become an important factor in appearance of many autosomal recessive, congenital anomalies and mental disorders. Health education and awareness regarding ill effects of consanguinity and preconception screening tests to the youth who are the pillars of society would have a great impact in decreasing the magnitude of prevalence and associated ill effects of the above.

Materials and Methods : A cross sectional study among 250 medical and 250 non-medical students was done where a questionnaire on knowledge, attitude and practice of consanguineous marriages was given and statistical analysis was done.

Results :
84.3 % medical students and 42.1% non-medical students were aware about consanguineous marriages causing birth defects in children. 0.4% medical students and 4.8% non-medical students answered that the consanguineous marriages had lower risk than non-consanguineous marriages. 24.1% medical students and 25.2% non-medical students opine that preconception carrier screening test is necessary only for consanguineous couples. 3.6% students still thought that consanguinity is a wise choice. 84.5% of the total students wanted to spread awareness about the ill effects of consanguinity.

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Conclusion : Increasing awareness among adolescents regarding hazards of kinship would prevent them from preferring consanguineous marriages. Providing knowledge about preconception genetic counselling encourages students to avail the benefits of it in the future and making carrier test screening centres more accessible to common public can change the prevalence and status of consanguineous marriages.

Aims & Objectives

1. To assess the knowledge of the study population regarding consanguinity, its associated congenital defects and preconception carrier screening.
2. To assess the attitude of the study population regarding consanguinity, its associated congenital defects and preconception carrier screening.
3. To assess the practice of the study population regarding consanguinity, its associated congenital defects and preconception carrier screening.

Introduction

Consanguinity refers to union between two blood related individuals who share a common ancestor.[1,2] Consanguineous marriages have been practiced since the early existence of modern humans.[3] It is a deeply rooted social trend in parts of the world like Saudi Arabia, Middle East , migrant communities in north, America, Africa.[4] More than one billion people of world are living in communities with preference of consanguineous marriage. This is more commonly seen in the rural areas, especially in the low socio-economic people, illiterates or with primary level education. [4]

This marriage system has been reported as an important factor in the appearance of autosomal recessive disorders, congenital anomalies including cleft lip, cleft palate, atrial septal defects, pulmonary stenosis, and pulmonary atresia. Yet these marriages are culturally preferred. The reason is ease of marriage decision making when the potential spouse is well known and considered to be a part of the extended family. What's more, these relationships likewise will in general strengthen social and kinfolk bonds starting with one then onto the next age. Reports from India and west demonstrated that consanguinity assumes a critical function in mental health issues. Every one of these issues assume a critical part on world economy and efficiency and become a colossal weight on clinical organization. Regardless of clinical progressions, proficiency rate urbanization, still this age old customs can't be broken.[5]

The risk for birth defects among offspring of first cousin matings has been increased to 5 to 8% compared to 2 to 3% in non-consanguineous marriages [6]. Consanguinity rates shift from one population to another depending upon religion, culture and topography.

Health education is a significant method for improving the public impression of recently introduced health interventions. Preconception genetic counselling and screening test for consanguinity is considered one of the important pillars amongst the community genetic services in highly consanguineous couples.[7] A research conducted in Andhra Pradesh on premarital genetic investigations and effects of genetic counselling, consanguinity was found in 86.04% cases while 73.25% presented family history of different genetic disorders. [8]

The present study is a preliminary one to obtain first-hand information about the magnitude of the problem in our state. The future predominance and status of consanguineous marriage is a matter of conjecture.

Methodology

Study Design: Cross-sectional study

Study Type: Observational Study

Study Tools: Semi-structured questionnaire [2,3,9,10,11]

Study Area: One engineering and one medical college in Hyderabad

Study Period: One month from the date of approval by ethical committee

Study Population: Students of the respective colleges

Sample Size: 500 - 250 medical and 250 non-medical students

Inclusion Criteria:

1. Medical and non-medical students between the ages 18-25.

2. Students who have given their consent.

Exclusion Criteria:

1. Students who don't know English.

Methodology

After receiving a verbal consent, the involved students were given a questionnaire written in English. The questionnaire contained questions on knowledge, attitude and practice of consanguineous marriages. The statistical analysis was done using excel 2010 and epi info version 7.2.

Results

Participants : The sample size was calculated as a minimum of 423 assuming 95% confidence level, 5% error, 50% proportion of poor level of knowledge and 10% non-response rate. We visited various colleges offering medical and nonmedical courses. Every student in a registered college was eligible for the study. Each student was examined for eligibility. Candidates who were between in ages of 18-25 were included in the study. Students who were not willing to give consent and could not read and write English were excluded from the study. The total number of candidates confirmed eligible were 500. The total number of responses analysed is 500. (Follow flow chart Fig-1)

Fig.-1

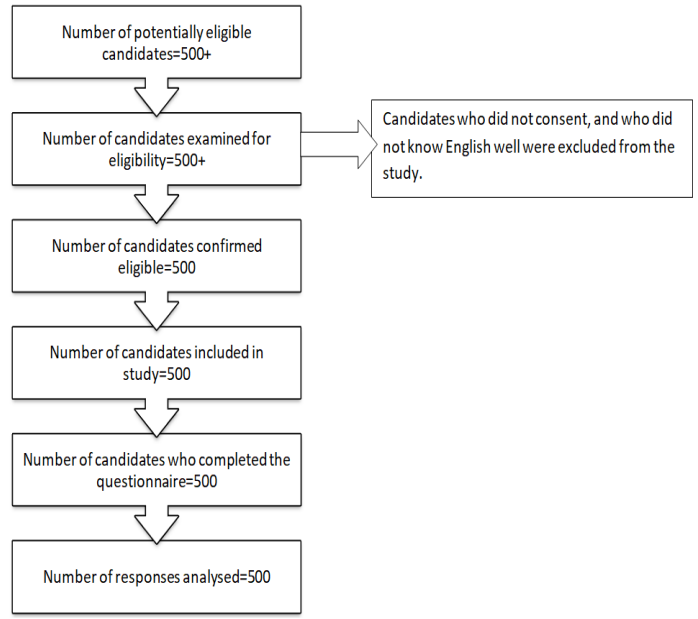


Table-1

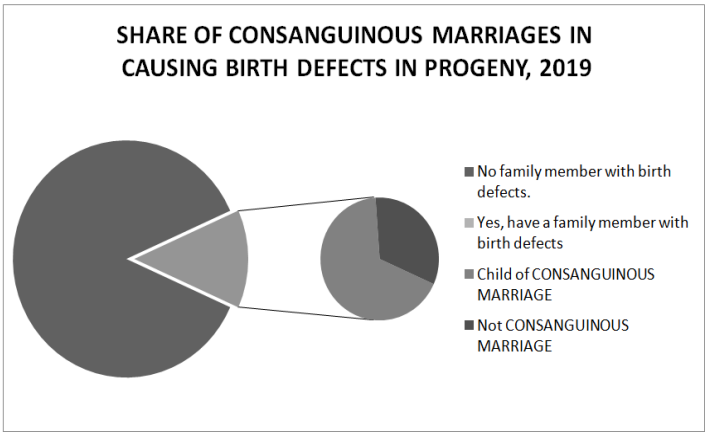
SOCIO-DEMOGRAPHIC CHARACTERS	MEDICOS	NON-MEDICOS	TOTAL
Age			
a) 18-20	224(89.6%)	230(92%)	454(90.8%)
b) 20-22	22(8.8%)	14(5.6%)	39(7.8%)
c) 22-24	2(0.8%)	2(0.8%)	4(0.4%)
d) 24-26	0(0%)	0(0%)	0(0%)
Gender			
a) Male	70(28%)	139(27.8%)	209(41.8%)
b) Female	180(36%)	111(22.2%)	291(58.2%)
Education of the head of family			
a) Illiterate	4(1.6%)	16(6.4%)	20(4%)
b) Primary school	7(2.8%)	9(3.6%)	16(3.2%)
c) Middle school	7(2.8%)	15(6%)	22(4.4%)
d) High school	20(8%)	33(13.2%)	53(10.6%)
e) Intermediate	35(14%)	53(21.2%)	88(17.6%)
f) Graduate/Post graduate	157(62.8%)	118(47.2%)	275(55%)
g) Honors'	20(8%)	6(2.4%)	26(5.2%)
Family income			
a) <6327	4(1.6%)	13(6.2%)	17(3.4%)
b) 6327-18949	26(10.4%)	34(13.6%)	60(12%)
c) 18949-31589	22(8.8%)	34(13.6%)	56(11.2%)
d) 31589-47262	30(12%)	36(14.4%)	66(13.2%)
e) 47266-63178	48(19.2%)	51(20.4%)	99(19.8%)
f) 63182-126356	64(25.6%)	53(21.2%)	117(23.4%)
g) >126356	56(22.4%)	29(11.6%)	85(17%)
Religion			
a) Hindu	215(86%)	228(91.2%)	443(88.6%)
b) Muslim	24(9.6%)	7(2.8%)	31(6.2%)
c) Christianity	8(3.2%)	14(4.41%)	19(3.8%)
d) Sikhism	0(0%)	0(0%)	0(0%)
e) Buddhism	2(1.2%)	1(0.8%)	3(0.6%)
f) Jainism	0(0%)	2(0.8%)	2(0.4%)
g) Atheist	0(0%)	0(0%)	2(0.4%)
Permanent Residence			
a) Urban	220(88%)	187(74.8%)	407(81.4%)
b) Rural	30(12%)	63(25.2%)	93(18.6%)

Descriptive Results:

The study population was 250 medical and 250 non-medical students. Males represented 41.8% (209), while females represented 58.2% (291) with age range of 18-25 years (mean age=19.28). Out of them 81.4% were from urban areas compared with 18.6% from rural areas. 10.4% of the students stated that their parents were consanguineous. See table -1 for all the socio-demographic data of the candidates.

There are 12 students who had high prevalence (>5) of consanguineous marriages in their family. 14.8% had a moderate prevalence (3-5) of consanguineous marriages in their family. Prevalence of consanguineous marriages in our study is 18.5% out of which 61% had birth defects in their children. Refer chart Fig-2

Fig-2



Outcome results: A structured questionnaire, which was developed after literature review. The questionnaire was assessed by 3 experts. The questionnaire consisted of 30 items (9 demographic, 1 source of information, 1 opinion on reasons for consanguineous marriages, 4 history of consanguineous marriage in family, 7 knowledge, and 6 attitude questions and 2 questions analysing the practice) (questionnaire in supplementary file 1). The questionnaire was validated by doing a pre-test. Each correct answer was awarded 1 mark and wrong answer 0.

Knowledge

5 questions were asked to understand the knowledge regarding the existence of consanguineous marriages and the various birth defects it might cause in their offspring. Responses to questions related to knowledge were graded on a 3-point Likert scale, an agreement scale ranging from '1' for disagree to '3' for agree. (Refer table -2)

Table-2

ITEMS	MEDICAL STUDENTS	NON-MEDICAL STUDENTS	TOTAL
KNOWLEDGE			
GENERAL KNOWLEDGE ABOUT CONSANGUINITY			
1. Do you know about consanguineous marriages?			
a) Yes	248(99.2%)	228(91.2%)	476(95.2%)
b) No	2(0.8%)	22(8.8%)	24(4.8%)
The below questions have been answered by those who know about consanguineous marriages=476 included			
2. What is the health risk of consanguineous marriages?			
a) Lower in consanguineous(Disagree)	1(0.4%)	11(4.8%)	12(2.5%)
b) Similar in both(Neutral)	7(2.8%)	27(11.8%)	34(7.1%)
c) Don't know(Neutral)	11(4.4%)	78(34.2%)	89(18.7%)
d) Higher in consanguineous(Agree)	229(92.3%)	112(49.1%)	341(71.6%)
KNOWLEDGE ABOUT DISORDERS CAUSED IN CHILDREN BORN TO CONSANGUINOUS PARENTS			
3. Do you believe that consanguineous marriages may cause birth defects and genetics disorders in their children?			
a) Disagree	0	20(8.8%)	20(4.2%)
b) Neutral	39(15.7%)	112(49.1%)	151(31.7%)
c) Agree	209(84.3%)	96(42.1%)	305(64.1%)
4. Do you believe that consanguinity increases the risk of deafness, anomalies of extremities, and heart defects in their children?			
a) Disagree	7(2.8%)	14(6.1%)	21(4.4%)
b) Neutral	19(7.7%)	88(38.6%)	107(22.5%)
c) Agree	222(89.5%)	126(55.3%)	348(73.1%)
5. Do you believe that consanguinity increases the risk of blood disorders in their children? (eg. :beta thalassemia)			
a) Disagree	11(4.4%)	18(7.9%)	29(6.1%)
b) Neutral	27(10.9%)	95(41.7%)	122(25.6%)
c) Agree	210(84.7%)	115(50.4%)	325(68.3%)

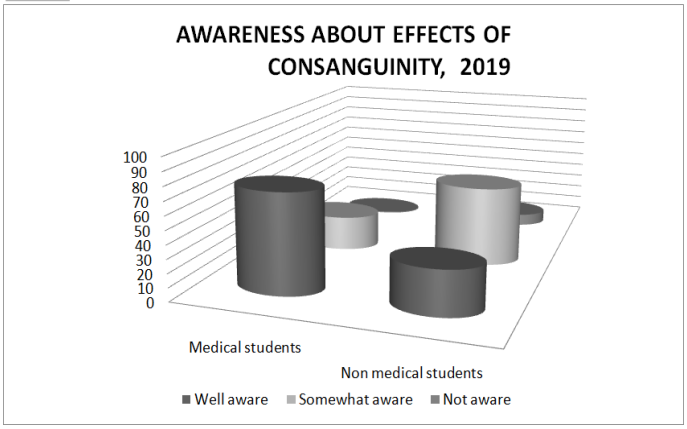
*All bolded squares are the right answers.

marriages than that of non-consanguineous marriages. 2.8% medical students and 11.8% non-medical students think that health risk is similar in both.

99.2% of medical students were aware of consanguineous marriages, while 91.2% of nonmedical students were aware (Refer chart Fig-3). (p=0.006).84.3% medical students were aware that consanguineous marriages causes birth defects and genetic defects in their off springs, compared to only 42.1% in non-medical students (p=0.002).

It was found to be statistically significant. A staggering 6.1% nonmedical students compared to 2.8% of medical students did not know if consanguineous marriages increase the risk of deafness, anomalies of extremities and heart defects in their children.

Fig-3



There were 2 questions to assess the knowledge about preconception carrier screening tests. Correct answers were awarded 1 point. (Refer table 3)

Table-3

ITEMS	MEDICAL STUDENTS	NON-MEDICAL STUDENTS	TOTAL
GENERAL KNOWLEDGE ABOUT PRECONCEPTION CARRIER SCREENING TEST			
1. Are you aware of pre conception carrier screening tests?			
a) Disagree(No)	171(68.4%)	203(81.2%)	374(74.8%)
b) Agree(Yes)	79(31.6%)	47(18.8%)	126(25.2%)
The below question has been answered by those who know about preconception carrier tests=126 included			
2. Do you think preconception carrier screening test has a role in controlling hereditary diseases?			
a) Disagree	1(1.3%)	8(17%)	9(7.1%)
b) Neutral	4(5.1%)	8(17%)	12(9.5%)
c) Agree	74(93.7%)	31(66%)	105(83.3%)

*All bolded squares are the right answers.

18.8% non-medical students and 31.6% medical students were aware about preconception carrier screening test. Participants' overall knowledge was categorized using modified Bloom's cut-off point. The knowledge was considered good if the score was between 80 and 100%, moderate if the score was between 50 and 79%, and poor if the score was less than 50%.(Refer table-4 for results)

Table-4

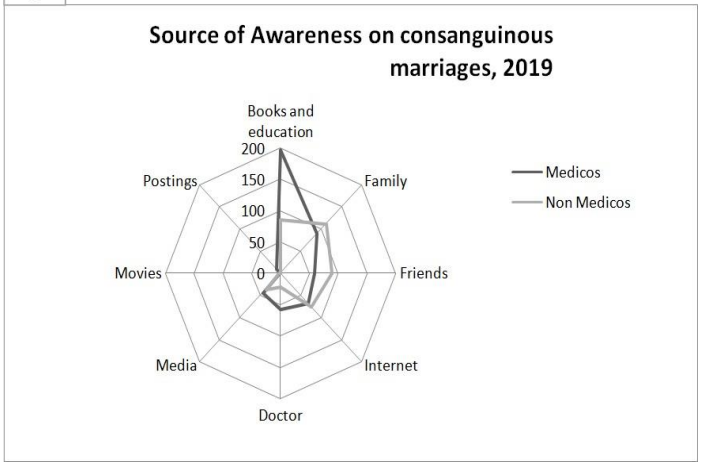
	MEDICAL STUDENTS			NON MEDICAL STUDENTS		
	Score achieved	Percentage	Inference	Score achieved	Percentage	Inference
Knowledge about consanguineous marriages	3.48/4	87%	GOOD	1.96/4	49%	POOR
Knowledge about preconception carrier screening tests	0.93/1	93%	GOOD	0.65/1	65%	MODERATE

Overall students exhibited a moderate level of knowledge about consanguineous marriages and a good level of knowledge about preconception carrier screening tests. The knowledge is better in medical students than non-medical students. Non- medical students had a poor level of knowledge about consanguineous marriages.

Sources of information

Figure-4 represents sources of information.

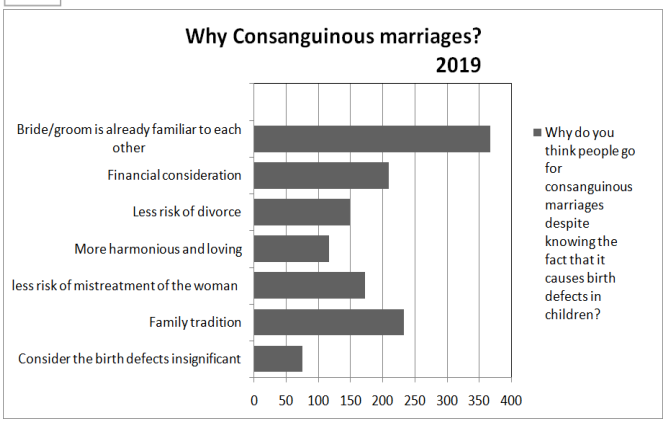
Fig-4



58.6% of the study population chose books and education as the prime source of information about the ill-effects of consanguineous marriages, followed by family (41.8%) and friends (30.6%).

Responses to "Why do you think people go for consanguineous marriages despite knowing the fact that it causes birth defects in children? (Refer Fig-5)

Fig-5



Attitude

Similarly, attitude towards consanguineous marriages and preconception carrier screening tests was assessed using 3 questions each. Correct responses were given a score of 1 and incorrect responses were given a score of 0. The overall level of attitude was categorized using original Bloom's cut-off point, as positive if the score was 80–100% , neutral if the score was 60–79% and negative if the score was less than 60%. A positive attitude towards consanguineous marriages and preconception carrier screening tests means having a perception of consanguineous marriages as a catastrophic public problem and the ill effects are preventable if appropriate strategies are devised such as preconception carrier screening tests.

Table-5 shows the attitude towards consanguineous marriages and table-6 is about attitude towards preconception carrier screening tests

Table-5

ITEMS	MEDICOS	NON-MEDICOS	TOTAL
ATTITUDE TOWARDS CONSANGUINOUS MARRIAGES- answered by those who know about consanguineous marriages =476 included			
1.Do you think consanguineous marriage is a wise choice?			
a) Yes, the risk is not significant.	6(2.4%)	11(4.8%)	17(3.6%)
b) It is the individuals will and choice.	41(16.4%)	44(19.3%)	85(17.9%)
c) Yes, if couples adopt children.	0	0	0
d) No, every child's health is important.	201(81%)	173(75.6%)	374(78.6%)
2.Do you think that the adverse effects of consanguinity should be made a part of the study curriculum?			
a) Disagree	8(3.2%)	29(12.7%)	37(7.8%)
b) Agree	240(96.8%)	199(87.3%)	439(92.2%)
3.Do you think mass campaigning about the hazards of kinship should be done on a community level?			
a) Disagree	2(0.8%)	30(13.2%)	32(6.7%)
b) Neutral	23(9.3%)	64(28.1%)	87(18.3%)
c) Agree	223(89.9%)	134(58.8%)	357(75%)

Table-6

ATTITUDE TOWARDS PRECONCEPTION CARRIER TESTS- Answered by those who know about preconception carrier tests=126 included			
1. What is your opinion on pre conception carrier screening test?			
a) It is not necessary	0	7(14.9%)	7(5.6%)
b) Necessary for all couples	60(75.9%)	28(59.6%)	88(69.8%)
c) Necessary for consanguineous couples only	19(24.1%)	12(25.5%)	31(24.6%)
2. Do you think pre conception carrier screening tests should be made more accessible and economical for the common public?			
a) Disagree	0	5(10.6%)	5(4%)
b) Neutral	6(7.6%)	7(14.9%)	13(10.3%)
c) Agree	73(92.4%)	35(74.5%)	108(85.7%)
3. Do you think the public should be made more aware about the preconception carrier screening tests?			
a) Disagree	1(1.3%)	5(10.6%)	6(4.8%)
b) Neutral	0	3(6.4%)	3(2.4%)
c) Agree	78(98.7%)	39(83%)	117(92.9%)

*All bolded squares are the right answers

Over all the students exhibited a positive attitude. The average score of medical students is higher than nonmedical students, especially about consanguineous marriages. Refer table-7 for results

Table-7

	MEDICAL STUDENTS			NON MEDICAL STUDENTS		
	Score achieved	Percentage	Inference	Score achieved	Percentage	Inference
Attitude towards consanguineous marriages	2.69/3	89%	POSITIVE	2.22/3	74%	NEUTRAL
Attitude towards preconception carrier screening tests	2.91/3	97%	POSITIVE	2.41/3	80%	POSITIVE

96.8% medical students compared to 87.3% non-medical students wanted adverse effects of consanguineous marriages to be made apart of study curriculum(p=0.00004)-statistically significant. Only 58.8% non-medical students compared to 89.9% medical students wanted mass campaigning about the hazards of kinship at community level. 25.2% of non-medical and 24.1% of medical students opine that preconception carrier screening test is necessary only for consanguineous couples, however 5.6% of the students opine that it is not necessary at all. 85.7% of the students think that preconception carrier screening test should be made more accessible and economical for common public.

Practice 2

We asked 2 questions to assess the practice of both groups. The results of the questions are given below in table -8

Table-8

ITEMS	MEDICOS	NON-MEDICOS	TOTAL
PRACTICE- answered by those who know about consanguineous marriages =476 included			
1. Would you like to spread awareness about the effects of consanguinity?			
a) Disagree	1(0.4%)	6(2.6%)	7(1.5%)
b) Neutral	25(10.1%)	42(18.4%)	67(14.1%)
c) Agree	222(89.5%)	180(78.9%)	402(84.5%)
2. Will you prefer consanguineous marriage?			
a) Disagree(No)	229(92.3%)	189(82.9%)	418(87.8%)
b) Neutral(Maybe)	17(6.9%)	37(16.2%)	54(11.3%)
c) Agree(Yes)	2(0.8%)	2(0.9%)	4(0.8%)

*All bolded squares are the right answers.

11.3% responded as maybe whereas 4 students, still want to prefer consanguineous marriages. 84.5% of the total students wanted to spread awareness about the ill effects of consanguinity. Over all the study groups had healthy practice.

Discussion

Consanguineous marriage is the relation between blood related individuals. These are widespread in North Africa, Central and West Asia and most parts of South Asia.[11] Many people turn a blind eye to the fact that consanguinity has a negative role on health of the progeny. Numerous studies show that congenital problems, birth defects, mental retardation, and other genetic diseases such as; sickle cell anaemia, thalassemia, haemophilia, congenital heart diseases, hearing deficit are common in these type of marriages.[12] First cousin marriages are the most common consanguineous marriages seen worldwide and it contributes the main reason for the congenital anomalies. [13]

The prevalence of consanguineous marriages varies worldwide. The rates of the consanguineous marriages are high in the Middle East, South, Central and West Asia.[16] Also in a study it was observed that in the Middle East, Pakistan had the most rates of inbreeding marriages (60%).[17] The rates of consanguineous marriages were reported to be 30.6% in Turkey, 28.9% in Egypt and 25% in Lebanon.[18,19]

It is important for us to impart this knowledge among young adults who are in the age of getting married. Not many studies have been done on students. Hence our study has been designed to assess the knowledge of young adults regarding this practice.

In a study in Prathima Institute of Medical Sciences (PIMS),76.9% of the medical students had knowledge on consanguinity, while in our study it was 99.2%. In a study done in Iran, it was reported that 44.6% of youth couples had poor knowledge about genetic consequences of inbreeding.[14] 10.4% of the students stated that their parents were consanguineous which was quite different to 41% in the study conducted in PIMS. [15]

Regarding health risk in consanguineous marriage in comparison to non-consanguineous marriage in PIMS, 92% found it higher and 4% lower in consanguineous marriages. This was slightly different to our study, where it was 71.6% and 2.5% respectively. 1.8% were not aware at all in PIMS which was quite contrary to 18.7% in our study.[15]

According to a study in Pakistan, the contributory factors to consanguinity include family pressure, low socioeconomic status, age at marriage, and cultural norms and traditions.[20] In our study 367 (73.4%) people think that the main reasons for consanguineous marriage is that bride/groom is already familiar to the family, financial consideration, family tradition and that it is more harmonious.

Increased awareness about consanguineous marriages will lead to a change in the attitude towards them. Community genetics will play an important role in fighting this cause. Preconception carrier screening is done to identify couples with an increased risk of having a child with genetic disorders before pregnancy, thereby enabling reproductive choices.

In our study population, a staggering 74.8% were unaware of preconception career screening test. Recent studies showed that the intended uptake of these tests by the general population varies from approximately 30% in the Netherlands and Sweden to as high as 68% in Western Australia.[21] This test aids in detecting any hidden genetic anomalies in the parents, thus helping the parents learn about the possibilities of healthy progeny. A poor knowledge of youth about these tests as inferred from our study brings forth the urgency for proper awareness and accessibility of them.

Conclusion

The students show moderate level of knowledge, positive attitude and good practice about consanguineous marriages. Medical students had a considerably higher knowledge and better attitude about consanguineous marriages.

The students show good level of knowledge, positive attitude about preconception carrier screening tests. Again the knowledge and attitude is better in medical students. The education about consanguineous marriages and preconception carrier screening tests must be increased especially for nonmedical students.

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PRAXIS UNDERGRADUATE MEDICAL RESEARCH JOURNAL

Review Article

Nanoscience in cancer treatment

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ABSTRACT

Nanomedicine is a unique interdisciplinary branch that integrates nanoscience and medicine to improve diagnostic abilities and treatment measures. The ability of nanoscience to synthesize a vast array of materials presents new avenues for developing diagnostic and therapeutic technologies. An important implication of this is in the field of cancer diagnosis and treatment. With the development of nanovectors, cancer chemotherapy now has advanced liposomal drug delivery systems at its disposal. Some nanovectors are, by themselves, used in chemotherapy. The field of cancer diagnostics has also benefitted greatly, since the targeted delivery of contrast agents using nanovectors has resulted in improved imaging modalities. The 'nanoarray', a version of the microarray having a millionfold increase in the information density, can simultaneously detect a large number of molecular species when used in cancer diagnostic technologies. The advent of newer nanomedicine-based platforms such as quantum dots, nanoshells, bio-barcodes, and implantable sensors is sure to revolutionise the field of diagnostics and therapeutics of cancer in the future.

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Introduction

In the current era, interdisciplinarity is becoming increasingly common in the field of medical research. Different disciplines have varied perspectives and approaches to the same object of inquiry. Thus, an interdisciplinary venture enables researchers to develop a more holistic solution to a problem, by integrating methods and tools of one discipline with the knowledge of another.[1] One such attempt is to integrate nanoscience and medicine for more effective diagnosis and treatment of diseases, leading to the rise of the field of 'nanomedicine'. Nanomedicine has diverse applications, ranging from drug delivery systems[2] and implants[3], to diagnostic and imaging tools.[4] This review article shall attempt to briefly describe the applications of nanomedicine in cancer.

About Nanoscience as A Field

Nanoscience refers to the study of the properties of matter at the 'nanoscale' level, with sizes in the range of 1-100 nanometres. It principally focuses on the unique, 'size-dependent' properties of solid-state materials. In other words, it is the study of structures and materials at an ultra-small level, i.e., on a scale of few nanometres, and the unique properties which these materials demonstrate. The physical and chemical properties of matter are very different at the 'nano' scale as compared to the 'macro' scale. It is an interdisciplinary field that incorporates knowledge and inputs from a variety of different fields such as chemistry, physics, biology, medicine, and engineering. Nanotechnology, also known as molecular manufacturing, is an extension of the knowledge of nanoscience used in the design and production of devices and systems at the 'nano' scale. In the words of Norio Taniguchi, the first person to use the term, "nanotechnology mainly consists of the processing of separation, consolidation, and deformation of materials by one atom or one molecule".[5]

The early 2000s saw a growing public awareness about the field of nanotechnology. In the years that followed, nanotechnology has been applied to human health with promising results, especially for treating cancers.

Technology in Nanoscience

The first progress in nanotechnology was made by the invention of STM (Scanning Tunnelling Microscope) which is used even today. This invention also led to the development of AFM (Atomic Force Microscope) and SPM (Scanning Probe Microscope) which are currently the instruments of choice for nanotechnology-related research.[5]
Other widely used techniques include-

• Nanoparticle synthesis- nanoparticles are synthesised by using either a bottom-up approach, which involves nucleating atomic-sized materials into the eventual nanoparticles, or a top-down approach, where bulk materials are broken down into smaller fragments which are then converted into nanoscale structures.[6]

• Electrospinning- a voltage-driven manufacturing process for creating electro-spun fibres and particles whose size ranges between a few nanometers to micrometers.[7]

• Cathodoluminescence (CL)- used for characterizing optical properties at the nanoscale which can then be used to explore many fundamental properties of the nanomaterial.[8]

• Nanoindentation- for measuring mechanical properties such as modulus and hardness of materials.[9]

• Langmuir Films- thin organic films with the thickness of one molecule. These serve as useful components in many practical and commercial applications such as sensors, detectors, displays, and electronic circuit components.

• Tensiometry- for measuring surface tension, contact angles, density, and other properties. This can be used to study the interactions between gas, liquid, and solid phases.

• Ion milling- it is a process of removing the top amorphous layer on a material to reveal the ideal surfaces for high-resolution imaging and post-processing.[10]

• Profilometry- a technique used to extract topographical data from a surface. It includes Optical, Confocal, and Stylus profilometry.[11]

• Quartz Crystal Microbalance- a highly sensitive balance that can measure mass changes in the range of nanograms.[12]

Materials such as carbon nanotubes, carbon dots, solid drug nanoparticle (SDN) formulations, biodegradable, and biocompatible comb-like polymers (CLBs), porphysomes, Peptide nanofibers (PNFs), Epigallocatechin gallate (EGCG) can be designed using techniques of nanotechnology.

The ability of nanotechnology to synthesise such a vast array of materials, makes it a promising avenue in the search for new methods of cancer diagnosis and treatment.

Nanoscience in Cancer Diagnosis and Treatment

Nanotechnology has evolved a class of molecules referred to as 'nanovectors'. These nanovectors are of interest for use in drug-delivery systems, improved imaging techniques, and visualisation of early molecular markers of disease, to name a few.

Nanovectors are generally classified into three 'generations'. The first generation comprises mainly liposomal delivery systems, which localise within the cancer lesions passively. The Liposomal Daunorubicin delivery system is one such example. Second generation nanovectors incorporated the concept of PEGylation, and the Enhanced Permeation and Retention (EPR) effect, to enhance the circulation time, stability, entrapment, and retention of the desired substance, resulting in products such as liposomal Doxorubicin (Doxil® - the first FDA approved nano-drug (1995)).[13] These can target their action by using antibodies, remote activation, or response to the environment. The third generation nanovectors are specifically designed to overcome different biological barriers and act on different subcellular targets, to perform functions in a time-sequenced manner with coordination between multiple, simultaneously released payloads of nanoparticles.[14]

With these these added 'tools' in the inventory of nanovectors, delivering more drug per biorecognition event as compared to immunotargeted drugs has become more efficient. Nanovectors also have a reduced clearance time, and hence decrease the toxic side effects caused by the persistence of drugs in the system. They also protect the drug against enzymatic degradation. By virtue of their properties, nanovectors can even allow drugs to cross barriers which earlier hindered their penetration, such as the blood-brain barrier, and vascular endothelium.[15] Since nanovectors can also carry imaging contrasts, they can be effectively used in targeted imaging modalities such as MRIs. Some nanoparticles themselves have image-enhancing properties.[16]

Nanovectors may directly be used in cancer chemotherapy. Nanoshells, which are metal-coated nanovectors, can reach highly specific sites of tumours, and be selectively activated by tissue irradiation. This would lead to thermal ablation, and the destruction of malignant tissue.[15]

Nanotechnology has been making headway in the domain of microarrays. 'Nanoarrays' allow a millionfold increase in the information density that can be packed in them, because the molecular depositions may now be controlled in the nanometre range. This has scope for detecting a large number of molecular species at the same time.[17,18]

The Future Ahead

Nanotechnology has a large potential for human use in the future, and a variety of platforms are under development. Quantum dots and nanoshells are being developed to improve MRI and CT scans in the imaging of cancer. Experiments have shown that some ligands can bind to apoptotic cells and hence, by monitoring apoptosis, the response to cancer therapy can also be monitored; for instance, the C2 domain of synaptotagmin and annexin 5 conjugated with iron oxide nanoparticles.[19] Similarly, research is also going on to improve implantable drug delivery systems to minimize peak plasma levels and reduce the frequency of re-dosing.[20]

Nanotechnology is also being tested to increase the growth and regeneration of nerve cells.[21] In-vivo early detection of cancer can occur using nanovector-delivered contrast agents involved in antibody targeting or signal amplification. For instance, Gadolinium carriers may replace sentinel lymph node biopsy. Implantable sensors may be designed, which prevent the non-specific absorption of serum protein ('biofouling'). Nanochips implanted with thousands of sensors made using nanowire, nanotube, and nanocantilever technology can be used to read the entire proteome and detect multiple diagnostic biomarkers. 'Bio-barcodes' are double-stranded DNA, with one end connected to a gold nanoparticle (AuNP), and the other to the analyte. These have a higher sensitivity and specificity than ELISA, and can be used in the rapid detection of trace analyte related to clinical medicine, food toxins, etc.[22]

In conclusion, the application of nanotechnology can revolutionise the field of cancer diagnostics and therapeutics. With rapid advancements in nanoscience, the interdisciplinary field of nanomedicine offers great potential for further research and development.

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PRAXIS UNDERGRADUATE MEDICAL RESEARCH JOURNAL

Review Article

Neurological Manifestations of COVID-19

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ABSTRACT

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is responsible for the global spread of coronavirus disease (COVID-19). Neurological complications are frequently reported in severely or critically ill patients with comorbidities. In COVID-19, both central and peripheral nervous systems can be affected. The SARS-CoV-2 virus enters the brain either via the hematogenous route or the olfactory system. Angiotensin-converting enzyme two (ACE-2) receptors, present on endothelial cells of cerebral vessels, are a possible viral entry point. Apart from pulmonary, cardiovascular, or hematological manifestations the neurologic system is also significantly impacted, with complications including acute cerebrovascular events, encephalitis, Guillain-Barré syndrome, acute necrotizing hemorrhagic encephalopathy. As the pandemic is spreading, there is a likelihood to observe more patients of COVID-19 either with neurological presentation or complications.

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Introduction

First appearing in Wuhan, China, severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) is responsible for the coronavirus disease of 2019 (COVID-19), which the World Health Organization (WHO) declared a pandemic in March 2020.[1] Although SARS-CoV-2 typically presents with pulmonary and/or cardiovascular complications, the clinician should be aware of neurological manifestations as it adds to the heightened morbidity and mortality. In COVID-19, both central and peripheral nervous systems can be affected. The following article is an attempt to review the neurologic complications from COVID-19.

Virus

A member of the β-Coronaviridae family, SARS-CoV-2 is an enveloped, non-segmented, single-stranded, positive-sense RNA genome, virus genome lies within a helical nucleocapsid, that is, surrounded by lipid bilayer capsule.[2–4]

Coronaviruses are zoonotic pathogens for humans and vertebrates, responsible for two outbreaks in the past: Severe Acute Respiratory Syndrome (SARS) and the Middle East Respiratory Syndrome (MERS)in 2002-2003 and 2012 respectively.[5]

Pathogenesis

SARS-CoV-2 virus entry, into the host cells, is a complex process. After binding to the receptor present on the host cell, the enveloped virus fuses its envelope with the host cell membrane; subsequently, the virus delivers its nucleocapsid into the host cell cytoplasm. In the host cell, viral RNA multiplies, and viral proteins are synthesized. Viral proteins reassemble with the viral genome, forming new virus particles. New virus particles are released in new uninfected cells, and thus, virus spread takes place.[6]

The SARS-CoV-2 virus utilizes the ACE2 for entry into the host cell. These receptors are profusely expressed on lung tissues and arterial and venous endothelial cells. ACE2 receptors are also expressed in the brain, particularly, in endothelial cells of cerebral capillaries.[7] A unique spike glycoprotein receptor binding domain of SARS-CoV-2 confers affinity of virus for an ACE2 receptor.[8] The binding of SARS-CoV-2 at the pulmonary epithelial cells also generates a global systemic inflammatory response (SIRS), producing increased levels of interleukin IL-6, IL-12, IL-15, and tumor necrosis factor-alpha (TNF-α); activating glial cells; and producing a massive pro-inflammatory central nervous system state.[9] In particular, IL-6 levels have been correlated with increased disease severity in COVID-19.[9] These systemic effects combined with localized lung alveolar damage result in severe hypoxia, which can lead to cerebral vasodilation and may decompensate into cerebral edema and ischemia.[9,10]

The virus, possibly, enters the brain either via hematogenous route or trans-neuronally via the olfactory system, across the cribriform plate.[11] The mechanisms by which SARS-CoV-2 causes neurologic damage are multifaceted, including direct damage to specific receptors, cytokine-related injury, secondary hypoxia, and retrograde travel along nerve fibers.[1]

Clinical Presentation and Diagnosis

The incubation period of COVID-19 is assumed to be between 2 and 11 days with an approximate mortality rate of 2 to 4 %.[9,12] As per the studies, during the incubation period, infected individuals produce a large quantity of the virus in the upper respiratory tract which leads to the latent spread of infection.[13].

Fever is the most frequent symptom. Fatigue, dry cough, anorexia, myalgia, dyspnea, and expectoration are other common initial symptoms.
Reverse transcription-polymerase chain reaction (RT-PCR) is the gold standard diagnostic procedure for confirming SARS-CoV-2 virus infection. Recently, IgM and IgG antibody tests to detect antibodies, against SARS-COV-2 infection in human blood, serum/plasma, have been made available.

Clinical features of COVID-19 associated neurologic disease

About 35% of COVID-19 patients develop neurological symptoms and in some, these may be the presenting symptoms[14]; moreover, pre-existing neurological conditions have been linked to more severe COVID-19 infections.[1] These manifestations can be considered as direct effects of the virus on the nervous system, para-infectious or post-infectious immune-mediated disease, and neurological complications of the systemic effects of COVID-19. In one national registry of 125 patients with COVID-19 and neurological or psychiatric disease reported over a 3-week period, 39 (31%) patients had altered mental status, which included 16 (13%) with encephalopathy (of whom seven [6%] had encephalitis), and 23 (18%) with a neuropsychiatric diagnosis, including ten (8%) with psychosis, six (5%) with neurocognitive (dementia-like)

syndrome, and four (3%) with an affective disorder. Notably, 77 (62%) patients had a cerebrovascular event: 57 (46%) ischaemic strokes, nine (7%) intracerebral hemorrhages, one (<1%) CNS vasculitis, and ten (8%) other cerebrovascular events.[15]

The reported neurological sign and symptoms of COVID-19 include headache, dizziness, confusion, acute cerebrovascular disease, epilepsy, ataxia, anosmia, ageusia, and muscle pain, demyelinating encephalomyelitis.[16]
Headache is the most common CNS symptom with the prevalence varying from 6.5 to 23%, and the mean prevalence of 8% in different studies.[17] Also, those in the intensive care unit were more likely to report dizziness.[18]
Seizures have been reported in patients with COVID-19 and neither of them had a past or a family history of epilepsy.[5]
The plausible hypotheses include invasion of the brain by the virus causing encephalitis[19] or inflammatory mediators causing neuronal hyperexcitability through activation of glutamate receptors.[20,21] Ageusia and anosmia were the first symptoms of the disease in the majority of the patients, usually appearing in the first 5 days of the illness.[22] COVID-19 may be associated with severe neurological symptoms of acute cerebrovascular disease, meningoencephalitis and encephalopathy, and acute Guillain-Barre syndrome.
A systematic review and meta-analysis also identified a 2.5 fold increased risk of severe infection among patients with prior stroke[23], and also increased mortality in those with Parkinson's Disease.[24] The neurological presentation may be varied and may involve both the central and peripheral nervous system.

Neurologic Complications Associated with COVID -19 infection:

Acute Cerebrovascular Disease

It remains one of the more common and serious complications seen in COVID-19 populations and it results possibly due to a coagulopathy. SARS-CoV-2 causes a global inflammatory response and a hypercoagulable state evidenced by increased D-dimers, prolonged prothrombin time, and disseminated intravascular coagulation.[25,26] SARS-CoV-2 can cause damage to endothelial cells, activating inflammatory and thrombotic pathways[27], leading to macrovascular and microvascular complications.[28] Cerebrovascular manifestations include both types of stroke (arterial and venous), ischaemia, and less commonly, hemorrhage. Quoting a retrospective study from Wuhan, cerebrovascular manifestations were reported for 13 (6%) of 221 COVID-19 patients[29], 11 (5%) patients developed ischaemic stroke, one (<1%) had intracerebral hemorrhage, and one (<1%) had cerebral venous sinus thrombosis. Another study from Italy reported that 43 (77%) of 56 SARS-CoV-2- positive patients admitted to one neurology unit had cerebrovascular disease; 35 had ischaemic stroke and 3 hemorrhagic stroke, and 5 had transient ischaemic attacks.[30]

ACE2 receptors regulate blood pressure and according to the studies, SARS-CoV-2 spike protein could interact with ACE2 receptors, leading to elevated blood pressure and increase the risk of cerebral hemorrhage.[31,32] Moreover, the dissemination of the virus in the cerebral microvasculature, causes damage to the capillary endothelial cells resulting in tear of the vasculature to cause parenchymal hemorrhage.[33] Additionally, COVID-19 patients have been reported to have thrombocytopenia and coagulopathy, both of which are contributory factors for secondary brain parenchymal hemorrhage.[34,35]

Most patients were older than 60 years, and many had known risk factors for cerebrovascular disease, especially hypertension, diabetes, hyperlipidemia, and vascular disease.[36] Interestingly, COVID-19 has also led to younger patients presenting with ischaemic stroke, including large vessel occlusions.[37] Cerebrovascular symptoms usually began at a median of 10 days (range 0-330 after the onset of respiratory illness.[1] Immediate anticoagulation with low-molecular-weight heparin has been recommended for patients with COVID-19, to reduce the risk of thrombotic disease[38], and this must be balanced against the risk of intracranial hemorrhage or hemorrhagic conversion of acute infarct. Once diagnosed with ischaemic stroke, patients should still receive the standard of care based on their institution with consideration of intravenous thrombolytic medications and endovascular thrombectomy in the appropriate clinical scenarios, without any alteration to intervention criteria.

Encephalitis and Encephalopathy

Encephalitis is the inflammation of the brain parenchyma, usually caused by an infection or the body's immune defences, clinically characterized by acute onset of fever, vomiting, seizures and altered level of consciousness. Neurological features mostly started from the time of respiratory symptom onset to 17 days afterwards, rarely preceding even fever or cough. The neurological

manifestations were typical for encephalitis, with irritability, confusion, reduced consciousness, neck stiffness, and psychotic symptoms.[36] The pathophysiology is unclear but may be related to edema secondary to inflammatory injury versus direct viral infection.[39] Brain imaging usually is normal, but in a few cases, signal intensity changes were observed in temporal lobes. No specific treatment exists for SARS-CoV-2, except aggressive supportive care and treatment of raised ICP.

In an interesting isolated case, SARS-CoV-2 virus-associated brainstem encephalitis has been described. MRI showed hyperintense signal changes in the brainstem and the upper cervical cord. Clinical manifestations indicated dysfunction of the medulla, pons, as well as the midbrain.[6] SARS-COV-2 leads to pneumonia and impairment of brain stem cardio-respiratory regulation center, both of which lead to hypoxia, which in turn may exacerbate the neural damage, leading to a deadly vicious cycle.[5]

Encephalopathy is a pathobiological process in the brain that usually develops over hours to days and can manifest as changed personality, behaviour, cognition, or consciousness. In patients with encephalopathy and COVID-19, in whom brain inflammation has not been proven, the wide range of other causes to consider includes hypoxia, drugs, toxins, and metabolic derangements.[36] Altered sensorium, in COVID-19, is associated with an increased risk of death.[6] Autopsy material from a patient who developed encephalopathy weeks after presenting with SARS showed edema, neuronal necrosis, and broad gliocyte hyperplasia.[40] Immunohistochemical staining showed that SARS- CoV-2 in the brain was associated with elevated expression of the cytokine, monokine induced by gamma interferon (known as MIG or CXCL9) and with infiltration of monocytes, macrophages, and T cells. These findings are consistent with viral CNS entry triggering the infiltration of immune cells and the release of cytokines and chemokines, which contribute to tissue damage.[36]

Acute necrotizing encephalopathy (ANE) is a rare, progressive neurodegenerative disorder characterized by multiple, symmetric areas of edema and necrosis in the CNS. It is known to be due to the uncontrolled release of cytokines during a febrile disease such as influenza.[41,42] ANE leads to disruption of BBB without direct viral invasion. ANE has recently been reported in a COVID-19 case.[41]

Acute Disseminated Encephalomyelitis and Myelitis

Acute disseminated encephalomyelitis is a syndrome of multifocal demyelination, typically occurring weeks after an infection, which generally presents with focal neurological symptoms, often with encephalopathy.[36] Spinal cord involvement is uncommon and is due to cytokine storm and exaggerated inflammatory changes. The association of COVID-19 and ADEM/myelitis is not common. Only a few case reports are available, and are treated with corticosteroids or other immunotherapies.

Ageusia and Anosmia

A complete or partial loss of smell sensation (anosmia) and taste sensation (ageusia) is the most frequent neurological manifestation, seen even in mild to moderate cases. Smell sensation is more severely affected than a taste sensation and in many patients was the first manifestation of COVID - 19.[6] Therefore, some researchers suggested that people with such symptoms may be possible carriers and should isolate themselves from others. Most patients gradually regain their sense of taste and smell as they recover from SARS-COV-2 infection.[5] The exact mechanism is not known but animal studies suggest that coronavirus can disseminate transneuronally into the brain through olfactory pathways and invade the olfactory neuroepithelium integrity through the expression of TMPRSS2 and ACE2 in sustentacular cells.[43,44]

Peripheral Nervous System Involvement:

Guillain-Barré Syndrome (GBS) and its variants

Guillain-Barré syndrome is a frequently encountered neurological complication of COVID-19. Zhao and co-workers described the first patient of Guillain-Barré syndrome in a patient with COVID-19.[45] GBS is an acute polyradiculopathy characterised by rapidly progressive, symmetrical limb weakness, areflexia on examination, sensory symptoms, and in some patients, facial weakness, although several variants exist.[36] It is often preceded by respiratory or gastrointestinal infections from a virus or bacteria. This progressive neuropathy has recently been linked to SARS-CoV-2 infection. The interval between the onset of viral illness and the first symptoms of GBS was between 5 and 10 days.[46] All patients presented with classical clinical manifestations – acute symmetric flaccid,

areflexic quadriparesis. CSF examination, in the majority, revealed albumin-cytologic dissociation. Treatment with intravenous immunoglobulins led to complete or partial recovery, in the majority and few patients needed ventilatory support.[6]

Miller-Fisher syndrome is a variant of Guillain-Barré syndrome and is characterized by ophthalmoplegia, ataxia, and areflexia. Miller-Fisher syndrome has also been described in patients with COVID-19.[6]

Skeletal muscle manifestations:

Myalgia, Rhabdomyolysis, and Myositis

General muscle pain or myalgia and fatigue are common initial symptoms of COVID-19 and its prevalence may be as high as 35%.[6] Creatine kinase levels were elevated in all patients with muscle disease. Furthermore, patients with muscle injury showed more signs of multi-organ damage, including more serious liver and kidney abnormalities, than patients without muscle injury.[46]

Rhabdomyolysis, a life-threatening disorder, has also been described in COVID-19. Rhabdomyolysis is clinically characterized by myalgia, fatigue, and hemoglobinuria. If not recognized and treated promptly, acute renal failure may set in.[34,47] A COVID-19 patient, presenting with localized muscle pain or generalized weakness, a high index of suspicion for rhabdomyolysis should be kept.[48,49] It has been hypothesized that the virus enters the muscles via the ACE2 receptor, and can cause muscle injury.[50]
Beydon and co-workers[53] have described myositis in a critically ill patient of COVID-19. The patient presented with acute myalgias, difficulty in walking, and proximal weakness. Creatine kinase level was markedly elevated.

Drugs

Many of the proposed drugs for use in COVID-19 have the potential to cause neurological toxicities. Lopinavir/Ritonavir and Azithromycin interact with many common medications in patients with prior strokes including antihypertensives, antiplatelets, statins, and anticoagulants.[1] These also carry an increased risk of neurocognitive impairment in longer courses. Ribavirin and interferon-α have both neuropathic and neuropsychiatric sequelae, while interferon carries a risk of retinopathy.[51] Similarly, antimalarials also carry the risk of neuropsychiatric side effects and less commonly ataxia, seizures, and limbic encephalitis.[52]

Conclusion

The COVID-19 pandemic has become a challenging global issue after its emergence in December 2019. Despite its most characteristic symptoms of respiratory distress, significant neurologic complications such as impaired level of consciousness, cerebrovascular disease, encephalitis, encephalopathy, and GBS have been reported from patients with severe COVID-19 infection. Several newly developed vaccines are currently in various phases of clinical trial. Exploring the neurological manifestations of COVID-19 is a step towards better understanding the virus, preventing further spread, and treating patients affected by this pandemic.

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