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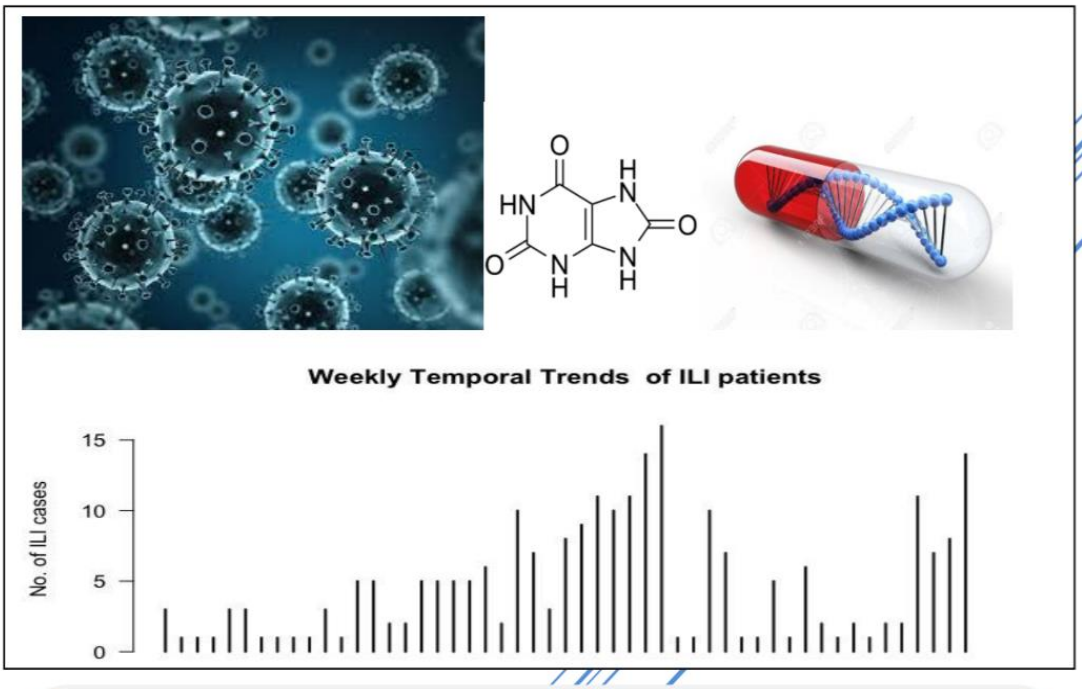

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COVID-19 and our DNA

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On December 31st 2019, Chinese Health Authorities in Wuhan city of their Hubei province, diagnosed 29 pneumonia cases of unknown etiology and informed WHO (World Health Organization). The unknown virus resembled SARS (severe acute respiratory syndrome), that occurred in China in November 2002, caused by a novel corona virus spilling over from an animal reservoir and transmitted by respiratory droplets. More than 8000 cases and 774 deaths were caused by SARS and circa US$20 billion coasted for its control (Whitworth, 2020).

Bionomic Studies:

Professor Chaolin Huang MD, with a team of 30 specialists in the field of epidemiology, clinical evaluation, laboratory testing, radiobiology and molecular-biology characteristics, as well as for treatment and clinical outcomes, started investigations. Researchers communicated directly with the patients or their families to ascertain epidemiological and symptom data.

By January 2nd, 2020, 41 isolated hospital admitted patients had been identified and confirmed through laboratory-testing by real-time RT-PCR and next-generation sequencing of having novel virus infection. It was established that these cases were associated with a seafood market where wild animals and live poultry were also sold. Environmental samples obtained from this market were found to be positive for Corona virus, suggesting a possible animal reservoir for this virus and zoonotic transmission, i.e., from animal to human; strengthening the hypothesis that it is a zoonotic virus. (Huang et al., 2020). Within a month it had spread throughout China and beyond. The Public Health Authorities conducted ACD (active case detection) finding and testing, contact tracing and quarantining of cases and contacts.

New Species of RNA Virus:

The virus was identified as a novel beta-corona virus and the genetic sequence revealed that it is a new RNA virus species, named "*SARS-CoV-2"* belonging to the family Coronaviridae of the order Nidovirales. Corona viruses are enveloped on-segmented positive-sense RNA viruses. They are broadly distributed in humans and other mammals. The infection is now officially termed COVID-19.

Outbreak of COVID-19:

The outbreak started moving from person to person - through contact (hand shaking, hugging and kissing), through vehicular transport from place to place, through international air travel, affecting neighboring and distant countries and it spread globally, like a wild fire, causing high morbidity and mortality. On January 30th 2020, WHO declared the pandemic a public health emergency of international concern. Thus, the outbreak became an extraordinary event of a public health risk requiring a coordinated international response. The current figures for the world, as on May 12, 2020, were: 4,318,171 infected; 1,569 recovered; 291,354 death. The figures vary from country to country due to ethnicity of the population and socio-cultural environment.

In Pakistan, the first case of COVID-19 was diagnosed in Karachi, on February 26, 2020, in a person came back after pilgrimage. The current figures as on May 12, 2020, were: 34,307 infected; 8776 recovered; 737 death. The scenario of infection rate - morbidity and mortality - is changing on hourly basis and the figures are rising constantly.

Management of COVID-19:

In the absence of treatment of RNA viruses, management and control the spread of COVID-19, health and administrative authorities in many countries enforced lock-out: educational institutions, local and intercity transport, industrial units, markets, restaurants, etc., were closed; religious and social congregation banned and people advised not to come out from their houses unnecessarily, however, the people are following the safety instruction half-heartedly. This technique slowed down the morbidity and mortality rates but with the passing days simultaneously enhancing the psychological stress and economic burden on the individuals and the state.

Print and electronic media presented all sorts of technical and non-technical persons in their columns and talk-shows emphasizing their point of view, which created confusion and panic.

Health System:

The existing health system in Pakistan is based on "Curative medicine" and the "Preventive medicine" is almost ignored. It appears that Epidemiologist is a very rare specialty in Pakistan, not visible taking part in the management of the pandemic. Perhaps there is none in any public health providing institutions in Pakistan.

IHPM:

In 1948, IHPM (Institute of Hygiene and Preventive Medicine) was established, containing M.B.B.S. and Ph.D. experts - Epidemiologist, Entomologist, Parasitologist, Public Health Engineer, Virologist, etc., - who were teaching and doing indigenous research, as well as, offering DPH, after a 2 year course in preventive public health, to students from East and West Pakistan. That was a right step in a country where 82.34% people are dying due to communicative, infectious and vector borne diseases (Khan et al., 1991).

Unfortunately, IHPH was converted into a College of Community Medicine in 1980. As a result of change, some posts were abolished, some never filled, while some were filled with irrelevant person, e.g., Parasitology was given to a Pathologist, Entomology and Epidemiology to simple untrained doctors. That was the end of Preventive Medicine in Pakistan. The existing expertise and infrastructure, capable and trained to manage public health problems and emergencies, disappeared with the passage of time. Since then to date neither Federal nor Provincial health authorities did anything to enhance preventive medicine capabilities in the country except taking isolated control programs, like Tuberculosis, Polio, Dengue, which are still extant.

1976 Epidemic:

On February 9, 1976, the whole country was shocked by the daily Pakistan Times headline: *"Doctors get it from patients"* and *"6 infected by danger virus"*. NHL (National Health Laboratories), now NIH (National Institute of Health) was assigned to investigate the outbreak. Col. M. I. Burny, then Director NHL, assured the nation that there is no danger of epidemic, Virus is Vector borne, vaccine likely, patients progressing, WHO virus expert arriving. However, Surgeon Matin Siddiqui and 2 others died, which created panic through newspapers depressing coverage. Even PMA (Pakistan Medical Association) urged Hazard Allowance for doctors. Government announced Rs 40,000 for the widow (worth 400 *tolas* of gold).

In the meantime, outbreak started moving south. A case reported from Hindu Chak, Gujranwala, alerted Brigadier Khawaja, Secretary Health Government of the Punjab, who asked Prof. Shamim Bukhari, Microbiologist to the Government of the Punjab, to attend an emergent meeting on the status of the unknown virus epidemic, along with relevant experts, for epidemiological investigations of this epidemic. During discussions in the meeting it ensued that the unknown virus clinical picture points towards CHFV (Crimean Haemorrhagic Fever Virus) that is transmitted by ticks, which explain the first case but not its southern movement, unless the patients were in Rawalpindi and had contact with infected ticks. On our request, Brigadier Khawaja instructed all the DHO (District Health Officers) to isolate suspected cases, draw 5 ml blood, cover the needle, put the syringe in a thermos flask containing ice and send it to Birdwood Road with a special messenger. We visited the probable source Takian village, district Rawalpindi, purchased a goat and got permission to draw blood samples from the flock, collected mosquitoes from all the spots, where cases were reported (from Rawalpindi to Multan). On testing, the collected material revealed low or high titer of the "danger virus". However, as we were exploring, forensic epidemiology pushing the probability of chance occurrence of the epidemic away, particularly as we recovered the danger virus from the Yellow Fever mosquito - *Aedes aegypti*, which is anthrophagus, does not normally feed on goat and not a vector of CHFV.

An Unbelievable Association:

Here we recall a first ever case, internationally, of a tick-borne virus from a mosquito. In 1966 we initiated a study on the bionomics of mosquitoes of CMNF (Changa Manga National Forest) to ascertain the species diversity and their bionomics - anthrophagy (feeding on human), zoophagy (feeding on animals), endophilism (resting in houses), exophilism (resting outside), etc. We found fauhal diversity of 29 mosquitoes species, some rare, some new to Pakistan, while all reported first time from CMNF. Various mosquito species pools were also used for virus isolation as nothing was known about the arboviruses and their vectors in Pakistan. In one pool of *Mansonia uniformis* mosquitoes a virus was isolated, which shocked our virologist Dr. Fatima Begum, who shaking her head in disbelief, said "how come that CHFV is present in a mosquito species while its natural vector is a tick" (Aslamkhan and Salman, 1969). Perhaps the mosquitoes were feeding on migratory bird roasting in CMNF. To verify it further we initiated a sero-epidemiological prevalence study for the presence CHFV antibodies in the resident population of CMNF. We were surprised with the result: circa 30% men possessed CHFV antibodies without any illness history - past or present. We hypothesize that the development of antibodies is the result of sublethal infection through ticks and/or mosquitoes in the forest workers. Final report was submitted to the Secretary Health Government of the Punjab, with the successful control of the outbreak without any further mortality, with the comments that probability of natural occurrence

of CHFV is null percent. To check the validity of COVID-19 our lab developed a PCR method to detect the novel virus, which is an open access article (Chaudhary et al., 2020).

DNA:

Life starts with a single cell that contain the complete sequence of our DNA, in the form of 23 pairs of chromosomes, one member of each pair comes from the mother, the other from the father. Chromosomes carry about 29,000 genes, which contain written information about our physical and mental characteristics; this DNA endowment is called genome. Human genome is 97% similar to gorilla and 98% matches with chimpanzee and only 0.5% differs with any other person. This difference is obvious with reference to reaction of corona virus latest novel species and human genome, as found by Prof. Huang results: The onset of infection commonly presented in these patient was as follows: fever 98%, cough 76%, and fatigue 44%. This means that the virus behaved differently with different person of the same ethnic group, all Chinese. Even the fever was not 100%, which points that 1 to 2 % positive cases may be treated as negative by thermal testing. The other common parameters, cough and fatigue, show more difference. RNA viruses cannot duplicate themselves. They require a genetically compatible host for their replication. We tested this hypothesis on HCV (hepatitis C virus) and found that circa 15 to 30 % men were totally resistant to HCV infection, 30 to 60 % patients were mildly susceptible, while 15 to 30 % were highly susceptible. COVID-19 may have the similar reactions with human DNA characteristics, which we are observing. The ultimate mortality rate may be from 0.09% to 2.09%.

COVID-19 is not spreading itself, we human are spreading it through contact and not following the safe hygiene procedures, as we followed in smallpox, which is now eradicated. Some basic research that lead to smallpox eradication, done in Lahore, was the absence of animal reservoir and that every new case lead to a trail of contacts. The cases were completely isolated till the recovery or death (mostly blood groups A or O). We neither know about the primary and/or secondary host of COVID-19 nor its prevalence. These information are important for control and management of an epidemic. To determine mammalian host, Universities can take up this research question. Prevalence can be determined through Cluster testing of 100 normal random persons in different parts of a city. The percentages of high infection could have given the priority areas for action.

Lock-out is not the solution as after lifting it after a week or month, the clean population will be exposed to the pathogen, that is present in “X number ?” of population, which we do not know. Health universities/institutions can do this research. There are many models to predict the persistence of infective agent, which will become ineffective after the population has achieved a herd immunity. Many countries have lost a large number of patients from their genetically susceptible population, and they are moving towards herd immunity.

The whole world is in a state of helplessness - strong or weak, rich or poor. There is no medicine to cure the COVID-19 and no state-of-the-arts hospital, in the most advanced country, can save you. People are praying according to their faith to save them from this “bla”. This is not a “bla” but a latest form of life by the almighty Creator.

I am thankful – *Alhamdulillah* - to the Creator of all life that this novel species is not “Air-Borne” otherwise we would have no place to hide ourselves. We Muslim, who claim that *Insan* (human being) are the best of all the creations - *“ashrafulmakhluqat”*, are now praying Allah to save us from this unseen creation. Are we the best of all creations - one may ask? The Creator informed us in Al Quran, sura *7. Al Isra*, verse 70 that *Insan* is better than most of the creations, but we insist that we are best of all. Let us read the translation by PICKTHAL:

“Verily we have honored the Children of Adam. We carry them on the land and the sea, and have made provision of good things for them, and have preferred them above many of those whom We created with a marked preferment.”

Instead of fighting with COVID-19, we must agree to its supremacy and keep ourselves away from it and plan for future health emergencies: Those who do not plan are planning for failure.

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Role of social Media in COVID-19 Pandemic

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Coronavirus disease 2019 (COVID-19) pandemic has produced a global health crisis that has had a deep impact on the way we perceive our world and everyday lives. Not only the spread rate of contagion and patterns of transmission endangered our sense of security, but the safety measures put in place to contain the spread of the virus also require social distancing by refraining from doing what is inherently human, which is to find comfort in the company of others. Within this context of physical threat, social and physical distancing, the role of the different mass media channels and social media in lives on individual, social and societal levels cannot be underestimated.

Social and mass media (broadcast and digital) has ability to convey a sense of unity by reaching large number audience/users. Social media may also provide grounds for misinformation and discrimination. People can utilize the flexibility and pervasiveness of social media technologies to increase the public's adherence to the safety measures suggested by global health organizations to combat the spread of COVID-19. Different media industries and channels for mass communication promote adaptive responses to foster positive health attitudes and adherence to preventive measures.

Social media can play positive role during the COVID-19 pandemic by promoting effective strategies for helping individuals in dealing with social and physical distancing and reducing stigma, prejudice, discrimination, and inequalities.

Social media like Facebook, twitter, YouTube, Instagram, snapchat and WhatsApp are major source for spreading information and news in public now a days but unfortunately in developing countries like Pakistan it creates more panic and spreading misinformation or fake news. Majority of the people who see misinformation about COVID-19 may think that what they are reading is true and can cause panic. People in Pakistan are inclined to share the misinformation and fuel the fear of something that isn't necessarily true. Misinformation, especially about COVID-19, can cause panic. People who see misinformation on social media may think what they are reading is actually true. Social media is the source of conspiracy theory that corona virus was developed to launch biological war against China for suppressing their economic growth. The rumors also spread through social media in China and other countries that corona virus was genetically engineered in bioweapons laboratory of Wuhan and then released worldwide which threatened the working relationship between Chinese and Western scientists for development of vaccine against COVID-19. In Iran the misinformation also disseminated through twitter that remedies which are not scientifically proven e.g. herbal products, drinks containing mint and spices like saffron offer cure against COVID-19.

During times of emergency and disaster, urgent questions arise and require immediate response. The problem in developing countries is that officials don't consistently provide the accurate information that's required very quickly. It is bitter truth in our society that subjective opinions and unverified claims spread rapidly through social and mass media in public than valid scientific and biomedical facts. The system how and why people should be held accountable for what they say in social media is weak.

In COVID-19 pandemic public officials are cautious about making premature pronouncements, instead carefully crafting statements to ensure accuracy and avoid the pitfalls of misinterpretation and exaggeration. Somewhat paradoxically, this careful approach may contribute to the formation of an information vacuum that rumors and falsehoods are all too ready to fill.

Governments can advertise through mass media to refrain the people from posting anything on social media about COVID-19 that makes fun of, ridicules, or minimizes the situation. Public health personnel, teachers, religious and political leaders must come forward to post about COVID-19 on social media that is informative and make sure that their followers know what's happening and the situation overall in their premises, local, National and international level.

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Spectrum of Mandibular Fractures in a Tertiary Care Hospital at Karachi

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Significance:
The maxillofacial areas are one of the most frequently fractured sites. With the mandible existence especially commonly affected due to its relative protuberance as associated with the rest of the facial skeleton. The management of these fractures is a task requiring skill and experience. In the repair of maxillofacial trauma, functional and aesthetic reconstruction is major concern. This study evaluated the frequency of mandibular fractures related to age, gender, etiology, and site in the last five years.

ABSTRACT

Objective: To evaluate the frequency, pattern, and etiology of mandibular fractures at a tertiary care hospital, in Karachi

Study Design: Retrospective, cross-sectional study.

Setting: Abbasi Shaheed Hospital, Karachi, Pakistan

Methodology: The study was initiated in Outpatient Maxillofacial Surgery Department of Abbasi Shaheed Hospital Karachi. The duration of the study was 5 years and six months. Data of mandibular trauma was evaluated. In this retrospective, cross-sectional study the patients were recruited through convenience sampling and the inclusion criteria was patients from both genders suffered from mandibular trauma of mandibular region. Patients who suffered from the trauma of face other than mandible were excluded. The sample size of the study was 464. A questionnaire was designed to enquire into the demographic details like age, sex, etiology, and site of fracture. The data was analyzed on SPSS version 17.0.

Results: The majority of patients were males i.e. 384 (82.8%) while 80 (17.2%) were females. The most common type of fracture was combination fractures followed by parasymphysis i.e. 142 (30.6%) and 79 (17%) respectively. Road traffic accident was the major cause of trauma i.e. 332 (71.6%) followed by fall 96 (20.7%). Cross tabulation was done between different variables. Association of gender with etiology and type of fracture revealed non-significant p-value while the association of age with etiology revealed significant p-value. The highest number of mandibular fracture cases due to RTA were reported in the year 2019.

Conclusion: It has been concluded that the frequency of mandibular trauma is quite high with male dominance. The most susceptible site of trauma is the combination and parasymphseal region and the most common etiology were road traffic accidents.

Introduction

The maxillofacial areas are one of the most frequently fractured sites. With the mandible existence especially commonly affected due to its relative protuberance as associated with the rest of the facial skeleton. The management of these fractures is a task requiring skill and experience. In the repair of maxillofacial trauma, functional and aesthetic reconstruction is our first concern. (1) These injuries can diverge in severity ranging from minor soft tissue injuries to major fractures of the whole facial skeleton. Fracture is not ever left ignored because it is very painful, pain that deteriorates with mastication and phonation movements, and even respiratory movements; sometimes there are facial asymmetry complaints. Mandibular fractures are informed to have an incidence of 15.5% to 59% amongst facial trauma worldwide and are the second most common facial fractures presenting to the emergency department. (2) The large inconsistency in reported incidence is due to a variety of contributing factors such as gender, age, environment, and socio-economic status of the patient as well as the mechanism of the injury. The most fortunate site of fracture (in descending order) in mandible are the body, angle, condylar region, symphysis, and coronoid process**.** (3, 4) Mandibular fractures may ensue alone or in combination with additional facial and skeletal bones. The etiology of mandibular fractures could be caused by road traffic accidents, accidental falls, assaults, industrial mishaps, sports injuries and firearm injuries. (5) Current trends in the management of mandibular fractures are, firstly, intermaxillary fixation only by dental wiring, arch bars and gunning splints. Also, intermaxillary fixation with osteosynthesis by transosseous wiring, circumferential wiring and external pin fixation. And, osteosynthesis without intermaxillary fixation by miniplates, non-compression plates, compression plates and lag screws. (6, 7)

Many studies have been done to evaluate the pattern and spectrum of mandibular fractures in different cities of Pakistan. (8, 9 and 10) The purpose of this study is to evaluate the frequency of mandibular fractures related to age, gender, etiology, and site in the last five years. This study also highlights the precautions to be taken in the prevention of mandibular fractures.

Materials and Methods

The study was initiated in the Outpatient Maxillofacial Surgery Department of Abbasi Shaheed Hospital, Karachi, Pakistan. The duration of study was six months and data of last 5 years was

evaluated. In this retrospective, cross-sectional study the patients were recruited through convenience sampling and the inclusion criteria was patients of any gender suffered from mandibular trauma of facial region. Patients who suffered from the trauma of face other than mandible were excluded.

The sample size of this study was 464 although a minimum sample size of 377 was calculated by Raosoft software with a confidence level of 95%, the margin of error 5% and response distribution of 50%.

A questionnaire was designed to enquire into the demographic details like age, sex, etiology, and site of fracture. The data was analyzed on SPSS version 17.0. Quantitative variables were calculated as mean and standard deviation. Qualitative variables like gender, the pattern of trauma, etiology were calculated as percentage. Chi-square test was used to evaluate the association of gender with pattern and etiology of trauma. p- value of < 0.05 was considered significant.

Results:

The results of the study revealed that the mean age was 27.24+13.564. The majority of patients were males i.e. 384 (82.8%) while 80 (17.2%) were females. **(Figure 1)**

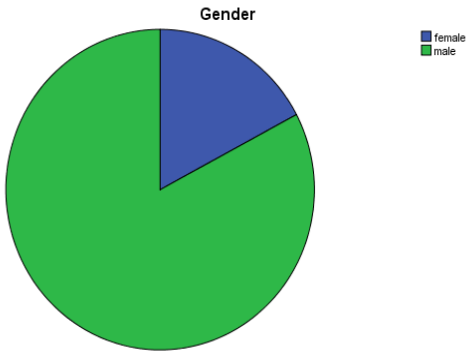

Figure 1: Percentage distribution of gender

The most common type of fracture was combination fractures followed by parasymphysis and condyle i.e. 142 (30.6%), 79 (17 %) and 75 (16.2 %) respectively **(Figure 2)**.

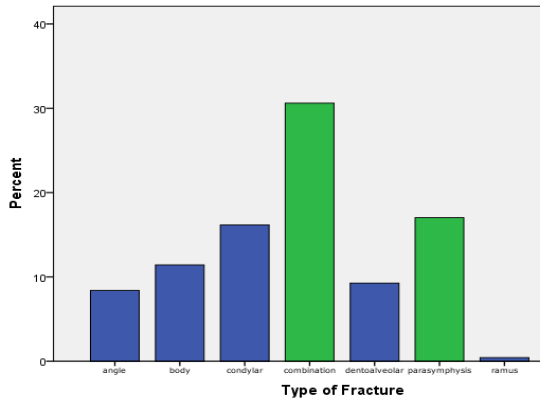

Figure 2: Percentage distribution of type of fracture

Road traffic accidents were the major cause of trauma i.e. 332 (71.6%) followed by fall 96 (20.7%) and assault 26 (5.6%). **(Table 1)**

Table 1: Percentage of Etiology of Mandibular Fractures

Etiology	N (%)
Assault	26 (5.6%)
Fall	96(20.7%)
Gunshot	2 (0.4%)
Road traffic accident	332(71.6%)
Sports	8 (1.7%)
Total	464 (100%)

Cross tabulation was done between different variables. Association of gender with etiology and type of fracture revealed non-significant (p= 0.537, p= 0.673) while association of age with etiology revealed significant p-value (p < 0.001) **(Table 2)**

Table 2: p- value of Different Variables of Mandibular Fractures

Variable	p- value
Gender and etiology	0.537
Gender and type of fracture	0.673
Age and etiology	0.139
Age and type of fracture	0.000

The highest number of mandibular fracture cases due to RTA were reported in the year 2019 followed by 2015 and 2018**. (Figure 3)**

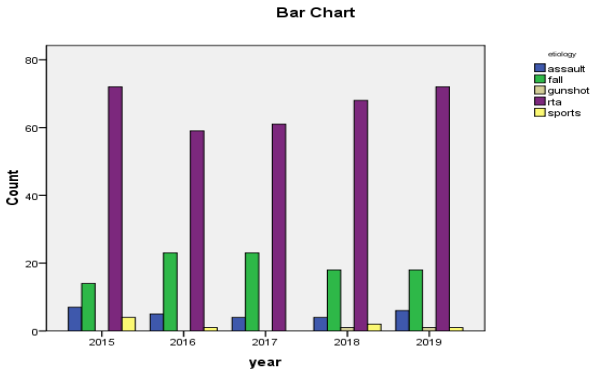

Figure 3: Yearly Distribution of Etiology of Mandibular Fractures

Discussion

The facial region is considered as one of the prone trauma sites among the human body. Amongst the face, mandible becomes the most susceptible site. (11) The results of this study revealed that the mean age was 27.24 ± 13.564. The majority of patients were males i.e. 384 (82.8%) while 80 (17.2%) were females. This is almost similar to the study conducted at Mayo Hospital Lahore, revealed that most patients were males (80%) and mean age was 26 ± 16.09. (12) Another study conducted at Abbasi Shaheed Hospital revealed that males constitute the

highest proportion of trauma victim especially mandibular fractures. (13) A retrospective analysis at maxillofacial trauma at a tertiary center in North West Ethiopia also revealed that males were 80% victims and their mean age range was 29.12 ± 8.62 years and the maximum age range of 21-30 years. (14)

The most common type of fracture was combination fractures followed by parasymphysis and condyle i.e. 142 (30.6%), 79 (17 %) and 75 (16.2 %) respectively. While a cross-sectional retrospective study conducted at Southern Taiwan revealed that condylar neck and head were the most common sites (32%) followed by the parasymphysis (21.7%), symphysis (19.5%), angle and ramus (17.5%) and body (9.3%). (15) In an epidemiological survey of mandibular fractures in Caracas (Venezuela) evaluated the incidence and its combination patterns showed that the parasymphysis region was the most common location of mandibular fractures with 144 (27.6%) fractures. (16)

A road traffic accident was the major cause of trauma i.e. 332 (71.6%) followed by fall 96 (20.7%) and assault 26 (5.6%). In a study published in 2014, by Elina M. Peltola, revealed that motor vehicle accident becomes the major cause of trauma among 374 patients. (17) A similar study conducted at Botucatu Medical College Clinical Hospital concluded that automobile accidents were the major cause which especially leads to multiple fractures of facial bones**.** (18) Another study also revealed similar results. (19)

Association of gender with etiology and type of fracture revealed non-significant p-value while the association of age with etiology revealed significant p-value. Logically evaluating gender does not have a significant part as accidents can occur anywhere and anytime without discriminating the gender and may affect any region of the facial area. While age has a strong relationship with trauma because the mean age in our study is 27.24 ± 13.564 with a wide range of standard deviation specifically in the male gender. This is similar to the study conducted at Jizan, KSA**.** (20)

The majority of males in this age group were motorbike riders and this youth of our population was frequently involved in reckless driving and one wheeling and prone to RTAs. The limitation of the study was a cross-sectional, retrospective study design.

It is recommended that awareness programs, talks, and seminars should be planned and executed to develop driving sense among the population. Strong implementation of traffic rules should be planned and drivers should be asked to strictly follow the vehicle driving regulations. Roads and bridges should be repaired, cleaned and constantly monitored for proper driving of the vehicles. Further studies should be planned in order to follow up with the patients.

Conclusion

It has been concluded that the frequency of mandibular trauma is quite high with male dominance. The most common reported were combination fractures followed by parasymphseal region fractures and the most common etiology was road traffic accidents.

Conflict of interest: Authors do not have any conflict of interest to declare.

Disclosure: None

Human/Animal Rights: No human or animal rights are violated during this study.

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General Health Status in patients of Adhesive Capsulitis Visiting Rehabilitation Department of Fauji Foundation Hospital Rawalpindi

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Significance:
Adhesive capsulitis is a serious condition which causes stiffness and disability to patients. Change in muscle tone and range of motion reduce the activities of daily living and disturb the sleep pattern. Current study investigated about general health status in patients suffering from this condition.

ABSTRACT

Objective: To investigate the general health status in patients of Adhesive Capsulitis

Study Design: Prospective study

Place and duration: Occupational Therapy Unit of Rehabilitation Department of Fauji Foundation Hospital Rawalpindi from July 1, 2019 to September 30, 2019.

Methodology: There were many patients suffering from shoulder pain. Among them, 52 patients who were suffering from adhesive capsulitis included. After the history of subjects, assessed for pain and restriction of range of motion in their affected shoulder. Lateral rotation, abduction, and medial rotation (LAM) test was performed. The inclusion criteria for subjects was symptomatic shoulder problems with restricted active and passive range of motion along with positive (LAM) test in ages between 30 to 80 years. The exclusion criteria was: (1) any neurological conditions affecting shoulder (2) any pathology other than adhesive capsulitis (3) any surgery of head, neck or upper limb. Data was analyzed using SPSS 25.

Results: Our study showed that all 52 patients were suffering from a very acute state of pain, sleep cycle disturbance, difficulty in activities of daily living (ADLs) and recreational activities. Some patients were jobless due to acute shoulder pain of adhesive capsulitis.

Conclusion: Adhesive capsulitis disturbs the daily life, sleep cycle, activities of daily living and difficulty in recreational activities. it is advocated that further researches must be conducted to point out the difficulties of such patients.

Introduction

Adhesive capsulitis is an extremely acute and serious painful state which causes stiffness and disability. It is typically clinically diagnosed disorder made on the basis of past history and physical assessment. It is a musculoskeletal condition due to vitiated soft tissue and articular capsule of glenohumeral joint of shoulder and characterized by inflammation and adhesions. (1) It has more frequency in females especially suffering from diabetes among ages of 40 to 60 years and 2 to 5% of population is affected by adhesive capsulitis. (2) Clinical features of adhesive capsulitis are acute which can disable an individual's ability to carry out daily activities at domestic and workplace. It costs a very significant economic loss with a lot of poor work performance. The shoulder joint is an essential to withstand heavy physical activity due to its ball and socket joint which provide a wide range of motion. (3) There are multiple etiological and referral factors which causes shoulder pain such as local pathologies, abdominal pathologies affecting the viscera, diaphragm and liver. Range of specific shoulder disorders as adhesive capsulitis are main cause of shoulder pain. (4) Shoulder joint provide wide range of motion and its extraordinary flexibility is due to scapulo-thoracic, acromioclavicular, glenohumeral and sterno-clavicular joints. support system of muscles and tendons supports the capsule within and outside of structure. This complex structure is more prone to injury, strain and sprain due to many idiopathic and secondary to other etiologies. (5) Pain, stiffness, or pain and stiffness both are main sources of physical impairment of shoulder joint result in sleep deprivation and other ADLs loss. It also has greatest influence to cause psychological and mood disorders such as anhedonia, depression and elation. (6) On inspection, the patient often presents acute pain while holding the arm in adduction and internal rotation. (7) Sometimes, atrophy of the shoulder muscles can be found. On palpation, there can be diffuse tenderness along the shoulder joint. There is a global restriction of movements of the shoulder, painful during early and middle stages of disease. Of particular importance is an almost complete loss of external rotation, which is almost pathognomonic. (8) This is confirmed by testing the active and, more importantly, the passive ranges of movement. Adhesive capsulitis is generally a clinical diagnosis and normally does not require extensive investigations. Plain radiographs of the shoulder to exclude osteoarthritis of the joint or other pathologies are usually sufficient. Blood tests, including infection markers, are normal in true frozen shoulder. (9) Typically, three phases are seen as frozen shoulder progresses, described as “freezing, frozen and thawing”. These stages last for approximately two years, with initial onset over days or weeks. The initial phase (freezing) is characterized by marked pain and lasts approximately three months. (10) The frozen (adhesive) phase lasts for 3-9 months, with significant stiffness and pain at the extremes of movement. The thawing (resolution) phase lasts for 9-18 months, is relatively painless, with stiffness

improving steadily during this phase. Several authors have described frozen shoulder as a self-limiting condition that resolves in 12-36 months. (11)

Materials and Methods

We designed this prospective study after approval of the Research Ethical Committee of Fauji Foundation Hospital and completed the research goals in 90 days from July through September, 2019. We conducted the research at Occupational Therapy unit of the Rehabilitation Department of Fauji Foundation Hospital, Rawalpindi, Pakistan. Patient's data was collected who visited Occupational Therapy Unit of Rehabilitation Department of Fauji Foundation Hospital during July 2019 to September 2019 for patient's ADLs, recreational activities, sleep cycle and mood issues. There were many patients suffering from shoulder pain and visiting Rehabilitation Department of Fauji Foundation Hospital Rawalpindi but 52 patients were those who were suffering from adhesive capsulitis. After the history of subjects, assessed for pain and restriction of range of motion in their shoulder. Lateral rotation, abduction, and medial rotation (LAM) test was performed to confirm diagnosis. The inclusion criteria for subjects were symptomatic shoulder problems with restricted active and passive range of motion along with positive LAM test in age between 30 to 80 years. The exclusion criteria were: (1) any neurological conditions affecting shoulder, (2) any pathology other than adhesive capsulitis, (3) any surgery of head, neck or upper limb. Data was analyzed using SPSS 25.

Results:

Lateral rotation, abduction, and medial rotation (LAM) test was performed on all patients who visited Occupational Therapy Unit of Rehabilitation Department of Fauji Foundation Hospital Rawalpindi with acute shoulder pain. Among them only 52 patients showed positive (LAM) test. Out of these, 20 (62.5%), 7 (21.9%) and 5 (15.6%) were at stage 1, 2 and 3 respectively. All these patients were unable to wash their lower back with hands due to restricted movement and acute pain at shoulder joint. 7 (13.5%) patients were suffering from hemiparesis. 13(25%) patients reported sensory loss at their affected limb. 49 (94.2%) patients were able to complete range of motion partially and only 3(5.8%) were able to complete full range of motion at their shoulder joint passively. None of these patients can complete active Range of motion. All subjects reported sleep disturbance. 49 (94.2%) were in mild depression and 3 (5.8%) did not report any mood swings. Only 5 (9.6%) patients were able to sleep on affected side. 29 (55.8%) patients reported that shoulder pain had very severe impact on their life, 20 (38.8%) reported severe impact and 3 (5.8%) reported moderate effect. Among study subjects, 5 (9.6%) were suffering from moderate pain, 23 (44.2%) were suffering of mild pain and 24 (46.2%) did not feel any pain during rest. 8 (15.4%) patients presented very severe pain during ADLs, 29 (55.8%) presented severe and 14 (26.9%) presented moderate and 1 (1.9%) presented mild while performing any task. 4 (7.7%) reported difficulty in sleep every day in past month, 33 (63.5%) several days per week, 12 (23.1%) one day per week and 3 (5.8%) less than one day per week. 19 (36.5%) patients were suffering from very severe limitation to use their shoulder joint to perform any activity,25 (48.1%) faced severe limitation, 4 (7.7%) endured moderate limitation while 4 (7.7%) under mild limitation. 13(25%) out of 52(100%) patients were unable, 29 (55.8%) out of 52(100%) faced severe difficulty and 10(19.2%) out of 52(100%) were facing moderate difficulty in putting on or removing a pullover in last month.24(46.2%) out of 52(100%) patients were unable, 28(53.8%) out of 52(100%) patients confronted with severe difficulty while combing or brushing their hair. 22(42.3%) out of 52(100%) were unable and 18(34.6%) out of 52(100%) faced severe difficulty ,9(17.3%) out of 52(100%) faced moderate difficulty and 3(5.8%) out of 52(100%) faced mild difficulty to reach shelves overhead. 32(62.7%) out of 52(100%) patients were unable, 19(37.3%) out of 52(100%) were bearing severe difficulty to search or wash their lower back with their hands due to restriction at affected shoulder joint. 13(25.00%) out of 52(100%) were unable, 32(61.5%) out of 52(100%) faced severe difficulty and 7(13.5%) out of 52(100%) faced moderate difficulty while lifting or carrying a full bag of groceries by using affected side. 18(34.6%) out of 52(100%) were facing very severe limitation, 34(65.4%) out of 52(100%) were countering with severe limitation in shoulder functions while performing recreational activities. 11(21.2%) out of 52(100%) patients were unable, 37(71.2%) out of 52(100%) were facing severe difficulty to throw a ball over head. 6(11.5%) out of 52(100%) patients were unable, 46(88.5%) out of 52(100%) were facing severe difficulty in performing activity and were unable to enjoy and faced degree of limitation on their frozen shoulder side. 25(48.1%%) out of 52(100%) patients did paid work , 16(30.8%%) out of 52(100%) did work at home , 6(11.5%) out of 52(100%) were unable to do any work due to adhesive capsulitis complications and 5(9.6%) out of 52(100%) were retired and bound to house and they were not doing any task. 31(59.6%) out of 52(100%) patients unable to perform their usual work all days of last month, and 21(40.4%) were facing difficulty several days per week due to adhesive capsulitis. 20(38.5%) out of 52(100%) were facing difficulty all days and 32(61.2%) out of 52(100%) were facing difficulty in several days of per week to do work carefully and efficiently. 20(38.5%) out of 52(100%) patients were forced to shorter their work in all days of last month and

32(61.5%) out of 52(100%) were those whom have to shorter their work several days per week due to adhesive capsulitis. 33(63.5%) out of 52(100%) were those who changed their way of usual work all days of month and 19(36.5%) out of 52(100%) were those who have to change the way of their work several days per week. 31(59.6%) out of 52(100%) were at poor level of satisfaction and 21(40.4%) out of 52(100%) were fair level of satisfaction. 45(86.5%) out of 52(100%) were those who want to improve their acute state of pain and 7(13.5%) out of 52(100%) were those who were want to change daily personal and house hold activities as shown in supplementary table 1 (available online).

Discussion

In this study, we collected data of 52 patients visiting to Rehabilitation department of Fauji Foundation Hospital, suffering from adhesive capsulitis. Due to adhesive capsulitis, their life was very disturbed, and they were facing difficulties in sleep, mood, activities of daily living (ADLs), leisure's and recreational activities. All difficulties and disabilities were demonstrated due to shoulder pain. All pain and disability issues were corelated with psychological factors (anxiety, mood disorders as depression) and physical or personal parameters. Onset of their experience was attributed to acute, incomprehensible pain leading to disability. To sweep over these characteristics and retrieving functional capacity was their first choice. Understanding the etiology, distressfulness and likely results of this acute state were also essential to these patients. They felt a state of comfort while sharing their issues to therapist. Desire of hope and encouragement through this confrontation, was main source of their happiness.

Our study focused mainly on their daily living issues, mood and sleep disturbances, and other conventional experiences. These frontiers and way of our investigation of parts of all difficulties of these patients are basic strength and essence of our study. Recruitment of patients was done at that setting where they have been managed for adhesive capsulitis. We have to face some hurdles to recruit them for study such as first difficulty was the initial diagnosis of this condition, and approach them in a very busy clinical routine. This was a such type of study whose spectrum was not very wide as we included data from very few patients of a same territory.

As a matter of all-inclusive searching and our know-how, we have not found any literature with which our study results can be compared directly. (12)proposed a qualitative study of patient's perceptions and priorities living with primary frozen shoulder. He only focusses on conventional way of care of patients of adhesive capsulitis. (13)only interviewed the patients who were going to take a Bown Therapy for adhesive capsulitis and he explained the experimental aspects of daily living with adhesive capsulitis including pain, stiffness, sleep disturbances , all that was according to our own but his main concentration was on the effects of Bown Therapy instead of patient's activities of daily living , recreational and pain issues investigation. (14)

Hush was the first person who systematically critiqued literature from United States of America, Canada, United Kingdom and Scandinavia and only focus on Musculoskeletal Physical Therapy Intervention for adhesive capsulitis rather than to search out difficulties of patients. His study is also not comparable with our study due to his focus differences. Our study directly comprehends and embrace the difficulties and satisfaction level of patients of adhesive capsulitis. Following our study results which clearly revealed that adhesive capsulitis has a major impact on activities of daily living, recreational activities and satisfaction of patients of adhesive capsulitis.

Conclusion

Adhesive capsulitis disturbs the daily life, sleep cycle, activities of daily living and difficulty in recreational activities. It is advocated that further researches must be conducted to point out the difficulties of such patients.

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Disclosure: None

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Effect of Intravenous Phloroglucinol Injections upon duration of Active First Stage of Labor

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Significance:
Prolonged labor is held responsible for poor maternal and neonatal outcome. Due to lack of remedies and defined criterion for active interventions, prolonged labor is manipulated for justification of cesarean sections leading to their higher rates than ever before. Hence the main goal of present study is to explore ways and means to ease out the natural birth process.

ABSTRACT

Objective: In our part of the world, poverty and illiteracy has adversely affected our core objective of pregnancy i.e. healthy mother and healthy child. Exploring the role of a routinely used drug in reducing the duration of labor could be a breakthrough. Present study was planned accordingly to evaluate the effect of phloroglucinol (PHL).

Materials and Methods: It was a Randomized controlled trial conducted at Department of Obstetrics & Gynecology, Combined Military Hospital, Bahawalpur from January to June 2019. This study included 60 cases of age 18 to 40 years, having singleton pregnancy and in active first stage of uncomplicated labor. Patients with history of multiple pregnancies, obstetrical and surgical complications and cardiorespiratory diseases were excluded. The cases were placed randomly into Group A & Group B and given intravenous PHL and a placebo respectively. After this, duration of the first stage of labor was recorded in minutes from when there was 3-4 cm cervical dilatation with regular uterine contractions to complete cervical dilation i.e. 10 cm and descent of the presenting fetal part.

Results: Mean duration of active first stage of labor in experimental group A (230.20 ± 52.96 minutes) was significantly higher than that of control group B (345.30 ± 50.57 minutes).

Conclusion: This study concluded that intravenous PHL has efficiently reduced the duration of active first stage of labor in these randomly selected nulliparous and multiparous women. PHL is a useful drug serving the purpose of a spasmolytic, analgesic, and labor augmentation at the same time.

Introduction

Labor is the process of expulsion of products of conception (POC) that comprises of three successive stages viz cervical dilatation, fetal expulsion, and placental expulsion. (1) Regular and powerful uterine contractions initiate first stage of labor which includes a latent phase (insubstantial cervical effacement and cervical dilatation upto 5cm) followed by an active phase (substantial cervical effacement and complete cervical dilatation i.e. 10cm). The latent phase is prolonged if the duration exceeds 20 hours and 14 hours for primiparous and multiparous respectively. The active phase is considered prolonged if it exceeds 4 hours after adequate uterine contractions and 6 hours after inadequate uterine contractions. (2) Failure to progress spontaneously and deliver the POC is known as prolonged labor or dystocia but its more suitable to relate it with outcome or goals of pregnancy rather than simply the time duration. (3) One in every five of the women has to suffer from dystocia while almost 2/3rd of them are nulliparous. Other contributory factors include premature rupture of membranes, hypertension, hydramnios, over age, high BMI, epidural anesthesia and early hospitalization. (4)

White et al., interviewed the practitioners across Australia regarding "safe prevention of primary cesarean section" and could not find a consensus about when to augment labor medically or terminate labor through a cesarean section. They concluded with recommendations for further steps to remove barriers like basic policies, inadequate resources, women expectations about care and medicolegal issues. (5) According to statistics provided by World Health Organization (WHO) maternal mortality rate (MMR) and neonatal mortality rate (NMR) in Pakistan are 170/100,000 and 36/1000 live-births respectively. (6) This demographic data is very much alarming and UNICEF reported poverty, education and early age marriages as the main contributory factors, all of which lead to poor management of labor. In the country profile of Pakistan, UNICEF documented that sixty percent of NMR is the result of prematurity, birth trauma and birth asphyxia which are directly related to the delayed / obstructed labor. (7)

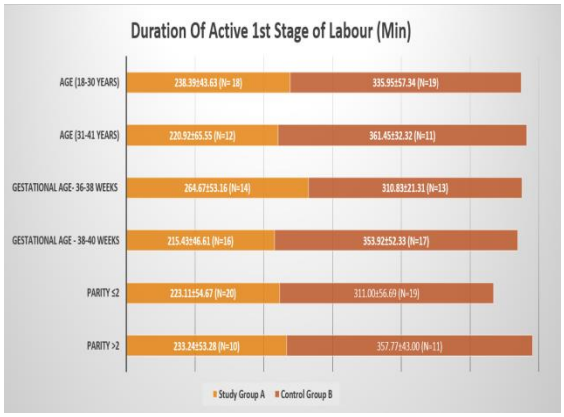

Fig 1: Duration of Active first Stage of Labor among various subgroups (Mean ± Standard Deviation

The efficacy of conventionally used oxytocin for augmenting normal labor is now questionable as it hasn't affected the worldwide reducing incidence of spontaneous deliveries and the researchers are keen to explore other drugs. (8) Phloroglucinol, labeled as 1,3,5- trihydroxybenzol (IUPAC) is a routinely prescribed spasmolytic agent. Inhibiting calcium influx into the smooth muscle cells has been linked to its probable mechanism of action however anti-cancer and anti-inflammatory role is being established recently as it has been recognized as modulator of prostaglandin release and oxidative stress. The current study is designed to determine its role in facilitating the process of labor through its smooth muscle relaxing property. (9, 10)

Materials and Methods

Eighteen to forty years old, sixty women with singleton pregnancy at gestational age 36-40 weeks were opted for the study. Women with multiple pregnancies, parity score >4, history of obstetrical and surgical complications and history of cardiorespiratory diseases were exempted from the study. The ethical guidelines i.e. approval from institutional research committee and detailed consent from the participants were strictly followed. The participants were randomly and equally distributed into study group A and control group B who were injected intravenous PHL 40mg (4ml) and intravenous placebo 4ml respectively at 0 hours. (11) Dose was repeated after 30 minutes. It was a double-blind trial as neither patient nor observer knew the content of the injection. The starting time of active first stage of labor was noted after regular uterine contractions and cervical dilatation of 3-4 cm. The duration was recorded over the monitoring chart until complete cervical dilation i.e. 10 cm or descent of the presenting fetal part, whatsoever comes first. All the data was entered and analyzed by using SPSS version 20.0. Mean and standard deviation was calculated for age, gestational age and duration of first stage of labor. Comparison between the groups with respect to the mean duration of first stage of labor was analyzed by student 't' test. P value ≤ 0.05 was considered as statistically significant.

Results

Mean duration of active first phase of labor in the study group A was 230.2 ± 52.96 minutes and in control group B it was 345.3 ± 50.57 min 345.3 ± 50.57 minutes. The difference was statistically significant (p value $\leq$ 0.05). Study participants were divided into two groups those were 18-30 and 31-40 years old and more participants from 18-30 years of age group.

Discussion

The results of present study have shown that PHL treatment significantly reduced the duration of active first stage of labor among the younger age group (18-30 years) and the elder age group (31-41years).

Similar findings were reported by Tahir et al., who investigated the effectiveness of PHL in preventing the cesarean section along with the parameters of fetal wellbeing (APGAR Score) and maternal wellbeing (Postpartum Bleeding) and declared the drug safe and appropriate for accelerating the normal labor process. (11) Naqvi and Haroon compared the role of PHL and drotaverine upon delayed normal labor and documented that both the drugs were beneficial while the effect of former was more significant. The researchers recommended the use of these drugs because of the analgesic effect and no feto-maternal adverse effect. (12)

The results of our study illustrate that PHL has reduced duration of active first phase of labor in pregnant women with gestational age ranging from thirty-six to forty weeks and the reduction is statistically significant. Tahira et al., also devised the same subgroups (based upon gestational age) and injected 40mg of PHL hourly after cervical dilatation of 4cm. The outcome was significant reduction of labor duration among the study group. (13) Our statistical data signifies the role of intravenously injected PHL in reducing the duration of labor among nulliparous women as well as the multi parous women. Janjua et al., investigated the role of PHL among the primigravida and compared it with drotaverine. first intravenous dose was given at cervical dilatation 4cm and second dose at cervical dilatation 8cm. Their results also concluded that women receiving PHL have shorter duration of normal delivery. (14)

Ara et al., conducted similar randomized double blinded controlled trial over hundred term primigravida cases and recorded the duration of first and second stage of labor. The study cases were injected with PHL and the control cases were given placebo. (15) The outcome was shorter duration of labor, lesser number of instrumental and cesarean deliveries among the study group. Parveen et al., assessed the role of PHL injection along with the conventional oxytocin infusion in women with delayed labor augmented by rupture of membranes and declared this regime safe and effective. (16)

Similar findings were reported by Tchente et al., who recently conducted a single blinded randomized control trial regarding the efficacy of PHL. PHL was found effective in achieving the primary goal i.e. escalation of delayed labor as well as the secondary goals comprising of fetal and maternal well-being. Also, there was no case of postpartum hemorrhage indirectly supporting the evidence that PHL doesn't inhibit uterine contractility. (17)

Contradictory to our comments Yuan et al., stated that PHL causes relaxation of uterine muscles and proposed its preventive role during threatened abortion. (18) Likewise, Xu et al., recommended therapeutic role of PHL for maintaining Invitro fertilization (IVF) induced pregnancy that is otherwise adversely affected by endometrial peristalsis. (19) Blanchard et al., reviewed the published data and

found insufficient for declaring PHL as an analgesic and antispasmodic agent in the field of gynecology and obstetrics.[20] These studies differ from the current study w.r.t stages of pregnancy; each of which has a distinct hormonal make-up and behaves differently.

Conclusion

Our statistical data concludes that the duration of active first phase of labor is significantly reduced by PHL as compared to the control group irrespective of the age, gestational week, and parity. It could be beneficial in facilitating delayed labor, in avoiding unnecessary cesarean sections and most of all reducing the MMR and NMR with minimal resources.

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Human/Animal Rights: No human or animal rights are violated during this study.

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The Impact of the COVID-19 Pandemic on the Utilization of Outdoor Services at Secondary Care Hospitals of Punjab, Pakistan

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Significance: Common mass are much afraid of acquiring COVID-19 infection. This fear led to less patient flow in hospitals of diseases other than COVID-19. This study is a valuable addition to the literature as it is the pioneer study to determine the impact of COVID-19 pandemic and lockdown on the OPD services at secondary care hospitals located province wide in Punjab Pakistan.

ABSTRACT

Objective: The objective of the study was to assess the effects of COVID-19 and lockdown on OPD services.

Materials and Methods: A cross-sectional study was conducted at District Headquarter Hospital (DHQ) and Tehsil Headquarter (THQ) Hospitals of District Layyah. The data was collected from one DHQ hospital and six THQ hospitals. The OPD data of three years (the years 2018 to 2020) was extracted from District Health Information System (DHIS). Trends of outpatients' flow during months of March and April of three years were taken. The data were analyzed using SPSS version 24.

Results: The COVID-19 pandemic was declared by World Health Organization (WHO) on March 11, 2020, and all countries started lockdown nationwide which imposed a major impact on all areas of life. Fear of coronavirus spread and lockdown resulted in significant reduction in number of patients at outdoor services. In our study, we analyzed outdoor services of seven hospitals of district Layyah - one DHQ hospital and six THQ hospitals.

Conclusion: Fear of coronavirus spread and lockdown resulted in significant reduction in number of patients at outdoor services.

Introduction

In December 2019, an increase in pneumonia cases of unknown etiology was first reported in Wuhan city of Hubei Province, China. (1) After one month, researchers separated a novel coronavirus (nCov) other than the viruses which cause severe acute respiratory syndrome (SARS), Middle East respiratory syndrome (MERS), avian flu, common flu, and other regular respiratory infections. (2,3) Later on, the novel coronavirus was named as severe acute respiratory syndrome – associated coronavirus-2 (SARS-CoV-2) and the following serious respiratory disorder as Coronavirus Disease 2019 (COVID-19). Since its flare-up, China reacted rapidly and took proactive general wellbeing measures to battle against the infection by serious reconnaissance, epidemiological examinations, dynamic treatment of affirmed as well as suspected patients, and prevention of rapid transmission. Nonetheless, virus had taken off to other countries before China limited it to its country. On January 30, 2020, World Health Organization (WHO) announced the disease as a Public Health Emergency of International Concern (PHEIC). (4)

The mode of SARS-CoV-2 transmission is yet not well-understood and new information is continuously being added to the literature. What is clear to date is that the mode of transmission is through contact or droplets, albeit airborne transmission has not been excluded. Since late January 2020, the Chinese specialists prescribed limited exposure of public to crowded places in order to prevent cross-infection. The individuals' dread of COVID-19 due to its novel and quick transmission made them hesitant to go to open spots including clinical and dental medical clinics. Among clinics, dental clinics were thought to be at high risk of COVID-19 spread as numerous dental procedures produce droplets or beads contaminated with blood and microscopic organisms such as viruses and bacteria, polluting the dental workplace as well as the workforce. (5) Therefore, members of social welfare in China requested to the dental organizations to deal with emergency cases only while suspending all other general and elective dental treatments. Strategic elements and individual contemplations resulted in reduced visits to dental outdoor patient department (OPD). Besides the dental clinics, the fear of COVID-19 spread might have reduced the general OPD visits. This study was conducted to assess the impact of COVID-19 and lockdown on OPD services in Punjab, Pakistan.

Materials and Methods

A cross-sectional study was conducted at District Headquarter Hospital (DHQ) and Tehsil Headquarter (THQ) Hospitals of District Layyah. The data were collected from one DHQ hospital and six THQ hospitals. The OPD data of three years (2018 to 2020) was extracted from District Health Information System (DHIS). Trends of outpatient's flow during months of March and April of three years were taken. The data were analyzed using SPSS version 24.

Results

The patients' flow at OPD during month of March and April 2020 of all hospitals was compared with those of month of March and April of 2018 and 2019. The purpose of this comparison was to check the effects of lockdown on outdoor patients' flow at the given hospitals.

DHQ Hospital Layyah

On comparison of OPD data during month of March and April of DHQ Hospital Layyah, significant reduction in outdoor patients during lockdown was noted. During month of March, 44,266, 59,700 and

37,751 patients were reported in the years 2018, 2019 and 2020, respectively. During month of April, 38,141, 58,008 and 19,508 were reported in the years 2018, 2019 and 2020, respectively.

As WHO declared COVID-19 as a pandemic, all countries started lockdown nationwide which imposed a major impact on all areas of life. Fear of coronavirus spread, and lockdown resulted in significant reduction in number of patients at outdoor services. In our study, we analyzed outdoor services of seven hospitals of district Layyah: one DHQ hospital and 6 THQ hospitals. We compared the OPD data reported in the months of March and April of 2020 with the OPD data reported in the months of March and April of 2018 and 2019. When we compared the OPD data reported in March and April 2020 of DHQ Hospital Layyah with those of March and April of 2018, there was 14.7% and 48.9% reduction in outdoor patients, respectively. Similarly, when the OPD data reported in March and April 2020 was compared with those of March and April of 2019, there was 36.8% and 66.4% reduction in outdoor patients, respectively.

THQ Thal Hospital Layyah

When we compared OPD data reported in March and April 2020 of THQ Thal Hospital Layyah with March and April of 2018, there was 16.9% and 49.4% reduction in outdoor patients, respectively. Similarly, when we compared the data reported in March and April 2020 with those of March and April of 2019, there was 24.6% and 59.4% reduction in outdoor patients respectively.

THQ Hospital Karor

Comparison of OPD data of March and April 2020 of THQ Hospital Karor with March and April of 2018, there was 38.3% and 77.6% reduction in outdoor patients, respectively. Similarly, when we compared the data reported in March and April of 2020 with those of March and April of 2019, there was 34.2% and 80.6% reduction in outdoor patients, respectively.

THQ Hospital Kot Sultan

OPD data reported in March and April 2020 of THQ Hospital Kot Sultan was compared with March and April of 2018, there was 88.3% and 52.8% reduction in

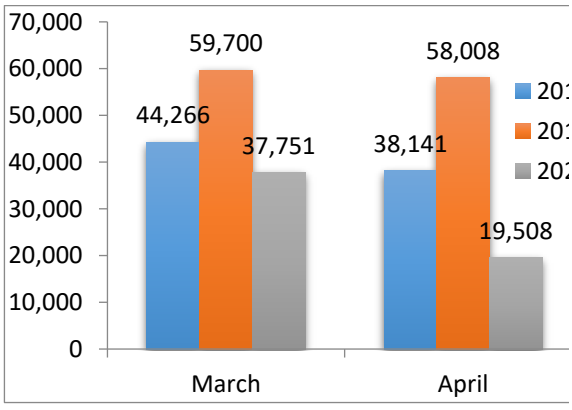

Figure 1: Comparison of outdoor patients of month of March and April of 2018, 2019 and 2020 at DHQ Hospital Layyah

Table 1: Effects of lockdown due to COVID-19 on outdoor services of hospital.

Hospital	No. of patients in 2020		No. of patients in 2019		No. of patients in 2018		Patient decline in comparison with 2018		Patient decline in comparison with 2019	
	March	April	March	April	March	April	March	April	March	April
DHQ Hospital, Layyah	37,751	19,508	59,700	58,008	44,266	38,141	-14.7%	-48.9%	-36.8	-66.4%
THQ Thal Hospital, Layyah	15,938	9,838	21,143	24,226	19,177	19,420	-16.9%	-49.4%	-24.6%	-59.4%
THQ Karor	15,541	5,641	23,601	28,993	25,175	28,360	-38.3%	-77.6%	-34.2%	-80.6%
THQ Kot Sultan	11,807	46,246	120,913	125,614	100,846	980,025	-88.3%	-52.8%	-90.3%	-63.2%
THQ Choubara	6,688	3,683	8,347	9,255	6,877	7,818	-2.8%	-52.9%	-19.9%	-60.2%
THQ Chowk Azam	16,438	9,838	20,557	24,159	22,028	22,880	-25.2%	-50.3%	-19.8%	-49.8%
THQ Fatehpur	9,841	23,934	16,475	17,415	17,837	17,703	-44.4%	↑35.2 %	-40.3%	↑37.4 %

outdoor patients, respectively. Similarly, when we compared OPD data reported in March and April 2020 with those reported in March and April of 2019, there were 90.3% and 63.2% reduction in outdoor patients, respectively.

THQ Hospital Choubara

While comparing OPD data reported in March and April 2020 of THQ Hospital Choubara with those reported in March and April of 2018, there was 2.8% and 52.9% reduction in outdoor patients, respectively. Similarly, when the OPD data reported in March and April 2020 was compared with those reported in March and April of 2019, there was 19.9% and 60.2% reduction in outdoor patients, respectively.

THQ Hospital Chowk Azam

Another comparison of OPD data reported in March and April 2020 of THQ Hospital Chowk Azam with those reported in March and April of 2018, there was 25.2% and 50.3% reduction in outdoor patients, respectively. Similarly, the comparison of OPD data reported in March and April 2020 with those reported in March and April of 2019 resulted in 19.8% and 49.8% reduction in outdoor patients, respectively.

THQ Hospital Fatehpur

Lastly, we compared the OPD data reported in March and March 2020 of THQ Hospital Fatehpur with those reported in March and April of 2018, we obtained surprisingly different results. There was 44.4% reduction in the month of March while 35.2% increase in number of patients in the month of April. Similar results were obtained when the data reported in month of March and April 2020 was compared with those reported in March and April of the year 2019, and significant reduction in the month of March (40.2%) and significant increase in month of April (37.4%).

Discussion

The purpose of this study was to assess the impact of COVID-19 pandemic and lockdown on the OPD services offered at secondary care hospitals. The study revealed significant reduction in patient outcome at OPD. During this deadly pandemic and lockdown, people were reluctant to avail OPD services.

According to our study results, the highest percentage of patient reduction was at THQ Kot Sultan (90.3%) in the month of March as compared to that of March 2019. A study by Guo et al. conducted at emergency dental services in China has reported 38% reduction in overall dental emergency patients. (6) Another study conducted by Lee et al. in South Korea in 2015 regarding MERS epidemic revealed 33.1% reduction in ER services during MERS epidemic 2015. (7) Similarly, a number of studies have revealed decline in utilization of healthcare services in different hospital settings. (8-10)

The present is a valuable addition to the literature as it is the pioneer study to determine the impact of COVID-19 pandemic and lockdown on the OPD services at hospitals in Punjab Pakistan. However, its limitations include its retrospective methodology and restricted single district study. However, studies at large scale might have revealed further insights on the outpatients' flow to the hospitals during COVID-19 pandemic and lockdown.

Conclusion

Fear of coronavirus spread, and lockdown resulted in significant reduction in number of patients at outdoor services. Reduction in OPD services during COVID-19 pandemic and lockdown at all hospitals was observed except at THQ Hospital Fatehpur where, interestingly, increase in number of outpatients was noted one month after lockdown. In a nutshell, COVID-19 pandemic and lockdown had significant impact on the OPD services at secondary care hospitals of Punjab, Pakistan.

Conflict of interest: Authors do not have any conflict of interest to declare.
Disclosure: None
Human/Animal Rights: No human or animal rights are violated during this study.

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Diagnostic Outcome of Open Pleural Biopsy

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Significance:
To diagnose pleural disease different biopsy techniques are available. Open pleural biopsy is used when a larger piece of tissue is required. Abnormal tissue growth is due to a virus, fungus, or parasite mesothelioma tuberculosis. Open Pleural biopsy is specified to improve the diagnosis of recurrent pleural effusion specifically when pleural carcinomatosis and tuberculosis is suspected

ABSTRACT

Background: Pleural diseases involve the parietal and visceral pleura. They can be of inflammatory or malignant origin. Pleural biopsy is advised for assessment and excluding infectious causes as tuberculosis or malignant disease, particularly malignant mesothelioma. Connective tissue disorders such as rheumatoid disease can also present with involvement of pleura, requiring pleural biopsy for diagnosis.

Objectives: The aim of my study was to find out diagnostic outcomes of open pleural biopsy or differentiation between benign (noncancerous) and malignant (cancerous) disease, to diagnose viral, fungal, and parasitic diseases of pleura.

Materials and Methods: Non-random sampling was used for data collection from Gulab Devi hospital. To find out the clinical value of nonspecific pleural biopsy specimen and fluid malignant neoplasm and tuberculosis. Data was collected from the patients undergoing procedure at Gulab Devi hospital. The collected data consists of 160 patients included females and males of all age groups.

Results: 160 patients were undergone biopsies. Out of 160 patients a nonspecific or normal result was found in 53(33.3%). Diagnostic of malignant neoplasm in 18(10.9%) and granulomatous disease in 28(17%). Tuberculosis was found in 46 (28.9%). Histopathologically, pneumonitis was found in 16 (10.1%).

Conclusion: Open pleural biopsy is precise and gold standard investigative method for malignancy. Pleural biopsy is safe easily performed and useful in diagnoses of tuberculosis or malignancy.

Introduction

The pleural biopsy is an investigative procedure in which membrane sample lining chest cavity (pleura) is obtained for examination. Pleura are a large, thin sheet of tissue that wraps around the lungs and lining inside chest cavity. Pleura layers have thin space filled with a small amount of fluid. (1)

The fluid helps the surfaces of parietal and visceral pleurae easily glide over each other during respiration. (2) The pleura is divided into parietal and visceral. The visceral layer is directly attached with lungs. The parietal layer is attached to thoracic cavity. The space between two layers is known as the intrapleural space. (3) The two pleural layers are separated by elasticity of the thoracic wall. (4)

The pleura is visible when there is abnormality. Pleural abnormalities can be subtle and it is important to check carefully around the edge of each lung where pleural abnormalities are usually more easily seen. (5)

Pleural diseases may be of either inflammatory or malignant origin frequently subsequent to pleural effusions. Pleural biopsy is required to reveal the cause of pleural effusion. The diagnostic procedures of pleural effusion include chemical, microbiological and cytological examination. Pleural biopsy is suggested for excluding infectious causes as tuberculosis and malignant disease particularly malignant mesothelioma. (6)

To diagnose pleural disease different biopsy techniques are available. There are three types of pleural biopsies such as closed open and thoracoscopic. In thoracoscopic biopsy endoscope is inserted to pleural cavity. Many diseases accumulate fluid in pleural space. (7) Risk increases with stress, obesity, smoking, chronic illness and the use of some medications (such as insulin, tranquilizers, and antihypertensive). (8)

Open pleural biopsy is used when a larger piece of tissue is required. Abnormal tissue growth is due to a virus, fungus, or parasite mesothelioma tuberculosis. (9) Open Pleural biopsy is specified to improve the diagnosis of recurrent pleural effusion specifically when pleural carcinomatosis and tuberculosis is suspected. (10)

This study was aimed to find out diagnostic outcome of open pleural biopsy performed at surgery department of hospital and histopathology was done for diagnostic purpose. The data was collected and analyzed to know diagnostic outcome of open pleural biopsy.

Materials and Methods

Settings: The data was collected from chest post-operative ward in Gulab Devi Hospital and study was completed at Gulab Devi Postgraduate Medical institute, Lahore

Study design: It was Cross sectional study design.

Duration of study: The study was completed in 5months from October 2015 to January 2016.

Sample size: We included 160 patients of open pleural biopsy.

Inclusion criteria: Patients in chest post-operative ward at Gulab Devi Hospital Lahore with open thoracotomy whom pleural samples were sent to histopathology lab for diagnosis were included in my study.

Exclusion criteria: Patient with close biopsy and/or open thoracotomy but samples were not sent for histopathology analysis.

Methodology: To determine diagnostic value of nonspecific pleural biopsy specimen in malignant neoplasm and tuberculosis data was collected from patients undergoing the procedure at Gulab Devi Hospital. The data collected consists of 160 patients both females and males of all age groups with different socioeconomic status. The data was collected within the duration of five months of all the registered cases. The data was collected with permission of concerned department and after approval of ethical committee on specially designed Performa. The data collected consist of the age and gender of patient, clinical appearance, and pleural diagnostic outcome. The data was collected and statistically analyzed.

Statistical Analysis: The statistical analyses were done in statistical package for social sciences (SPSS) version 16.0. Data was combined to perform analysis; categorical data are presented as percentage in graphs while descriptive frequency distribution was used for quantitative data.

Results

The patients mean age (year) with open pleural biopsy was 26.83±13.263.The male were 102 (63.75%) and female were (36.25%) with different age groups with mean age of 26.83±13.263 with maximum age of 70 and minimum of 8 years.

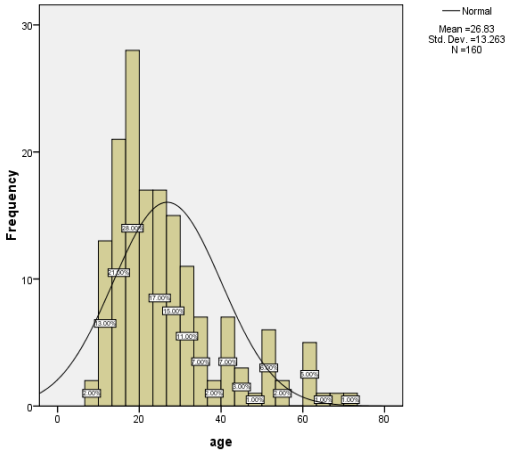

Figure 1; Descriptive statistics of age/years

Table 2.; Descriptive statistics of clinical manifestation of patients

	Total	Yes	No
Fever	160	129(80.65%)	31(19.35%)
Cough	160	143 (89.37%)	16(10.63%)
SOB	160	83(52.2%)	77(48.125%)
Pain	160	81(50.4%)	79(49.37%)
Weight loss	160	127(79.9%)	33(20.62%)

Out of 160 patients the 129 (80.65%) presented with fever, 143 (89.37%) with cough, 83 (52.2%) with SOB, 81 (50.4%) with pain and 127 (79.9%) presented with weight loss.

Out of 160 patients with undergoing the open pleural biopsy 46 (28.9%) with tuberculosis, 28 (17%) with granuloma lesion, 16 (10.1%) with pneumonitis, 18 (10.7%) with malignancy and 53 (33.3%) were diagnosed.

The descriptive statisctics of diagnostic outcome of patients undergoing diagnostic procedure is shown in Fig 2.

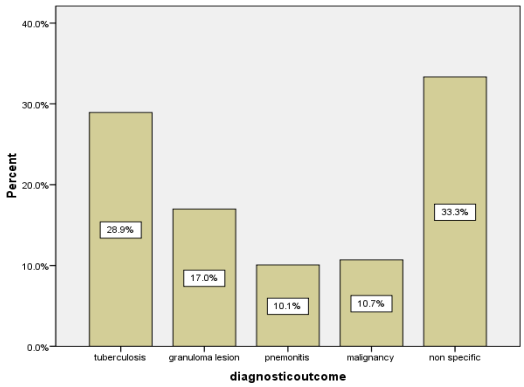

Figure 2; Descriptive statistics of diagnostic outcomes

Discussion

The pleura membrane is lining of lungs and chest cavity. The pleural biopsy is removal of pleural tissue for examination. Pleural biopsy is used to differentiate between benign and malignant disease. Majority of patients in this study were 20 to 30 years old or more. In current study, 71.4% of histopathologically proven tubercular pleural biopsy cases presented with chest pain, dry cough, breathlessness, and fever. It was observed breathlessness is the commonest symptom (30%) in cases of malignancy but our study reveals fever and cough to be the commonest symptoms (89.2%) followed by breathlessness and chest pain (61.5%). In our study, there was 28.9% and 10.7% cases of diagnosed tuberculosis and malignancy respectively. (11)

In pleural biopsy report, there was 5.6% cases with granuloma lesion but in this study 17% were diagnosed with granuloma lesion and 17.1 % diagnosed with pneumonitis. (12)

In another study of pleural biopsy established the cause of pleural effusion as malignancy and tuberculosis was in 22.4% and 31.1% cases respectively. In our study there was 46%with tubercular and 18% malignant histopathologically. When related with other studies, higher percentage tubercular and lower percentage of malignancy cases found in our study. (13)

The study of adequate tissue was done in 207 patients. Initially malignant neoplasm was diagnosed in 54 patients and granulomatous disease in ten. But in our study malignancy was diagnosed in 17 (10.7%) patients and granuloma in 28 (17%) patients. In

another study non-specific results were seen in 143 (68%). Malignant neoplasm and tuberculosis were eventually established in 30 excluded in 101 out of 143 patients. One false-positive result occurred in patient with nontuberculous granulomatous pleuritis. A definite diagnosis of tuberculosis and malignancy can be obtained by pleural biopsy.

Conclusion

Open pleural biopsy is precise and can be considered as gold standard investigative method for MPM. It is less sensitive for determining histologic subclass, particularly with nonepithelial subtypes. When thoracoscope is not available, pleural biopsy give definite diagnosis in significant cases of pleural effusion.

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Estimation of the Final Size of COVID-19 Epidemic in Balochistan

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Significance:

SIR model is used in this study to predict the magnitude of the disease in Balochistan from May 2020 on wards when lock down and other social distancing measures were loosened up by the government of Balochistan. Our Prediction model shows that about 30,00000 individuals in Balochistan will be infected by 5th of July 2020. Over all 25% of the total population of Balochistan will be affected by this disease with 98% (2940,000) recovery rate by the end of 15th July 2020.

ABSTRACT

COVID-19 is a new disease that is spreading very fast in Pakistan. Cases have been reported from all of the provinces including Balochistan. The first two confirmed cases in Pakistan had travel history by road from Iran to Balochistan, hence SIR model used to predict the magnitude of the disease in Balochistan from May 2020 on wards when lock down and other social distancing measures were loosen up by the government of Balochistan. Our Prediction model shows that about 30,00000 individuals in Balochistan will be infected by 5th of July 2020.Over all 25% of the total population of Balochistan will be affected by this disease with 98% (2940,000) recovery rate by the end of 15th July 2020.

Introduction

The first case of COVID 19 appeared in Pakistan in the month of Feb 2020, since than the infection has spread all over the country. Cases have been reported from all the four provinces including Balochistan. Since it is a new disease it is highly expected to become endemic in Pakistan very soon. The first case of COVID 19 in Pakistan had travel history by road from Iran to Pakistan, and it had to travel from Balochistan which is situated at the crossroad of trade route between Pakistan and Iran.

Since the government of Balochistan has relaxed the lock down measures from May 2020 it will have huge impact on the spread of the disease. Considering this situation, the SIR Mathematical modeling can play a key role in predicting the overall impact of COVID-19 in Balochistan.

SIR mathematical model is a compartmental model, it assumes the whole population of Balochistan into three compartments i.e. Susceptible (S), Infected (I) and recovered (R). Every individual in Balochistan will have to pass through all of these compartments.

SIR model operates under the assumption that the total population of Balochistan remains constant and no new births, deaths, in migrants and out migrants are included in the modeling. The model predicts the overall epi-curve by not taking into consideration several factors like age, gender, lock-down, quarantine and social distancing. The Recovery (R) compartment assumes a permanent immunity for the infected individuals and also consider the number of individuals that died due to COVID-19 into consideration. COVID-19 is a novel infection and not much is known about it. It may become endemic in Pakistan in near future. So far, no published study has surveyed the impact of COVID 19 in Balochistan.

Every infection follows a triangle of agent, host and environment. Every infection can classify society in to three categories i.e., susceptible, infected and recovered. Various factors come into play while considering such classification e.g., β**:** how often a susceptible and infected contact results in a new infection; γ**:** rate of an infected recovers and moves into recovery phase. (1)

Estimating the true picture of COVID-19 is essential. It could help us in decision making and policy guidelines, more over it would tell us the rate of spread and its potential of transfer from human to human. (2,4) In Wuhan the COVID-19 transmission started from the veterinary market. It is actually believed that this virus jumped from the bats to humans. Remission rate got severe day by day mostly affecting elderly showing symptoms while the young population remain asymptomatic. (3)

The R_0 for COVID-19 has been estimated between 2 and 4, with such rapid progression this infection was able to become pandemic. The disease is also deadly with almost 2% mortality rate. (5,9) Various phase adjusted estimates like sub-clinical, pre-clinical and clinical could possible explain the natural history of this disease but since most of the cases are asymptomatic hence it is very hard to classify and identify each and every carrier in a huge population, making it difficult to identify the cases. Event based surveillance system came up with a suspected case definition; every individual with fever, cough, and shortness of breath from experienced during the last 14 days, vaguely. (6)

The COVID-19 has shown little to no effect to various antibiotics used for the treatment; other clinical trials with controlled and blinded studies could potentially be able to produce a drug for this study. Hence, no effective treatment could be suggested to the critically ill individuals. (7) The Novel corona virus is a new disease; we can't surely state its symptoms and signs particularly when most of the individuals are asymptomatic. Major lessons learned are to use masks, protective gown, goggles, social distancing, hand washing etc. Because this virus is able to sustain

on surfaces for a longer period of time probably 12 days. (8,10)

Materials and Methods

A Mathematical Prediction Modeling conducted at District Quetta. The whole population of Balochistan (i.e., 12,344,408) was included in the study. Data was collected from daily situation report and analyzed through Vensim Software. SIR-Model Assumptions was used on this data. The model is built on the following set of assumptions, based on the methodology described by Ronald Ross and William Hammer 1, is expressed as the following differential equations:

$$dS/dt = -\beta ISN/N$$
$$dI/dt = \beta IS/N - \gamma I$$
$$dR/dt = \gamma I$$

Where S: Susceptible, I: Infected, R: Recovered, dt: Rate of particular disease and others as described above.

The basic assumption of the SIR model is that the total number of susceptible infected and recovered cases at any given time is equivalent to the test population, so the equations can be represented as:

$$S(t) + I(t) + R(t) = N$$

The basic reproduction number ($R_\circ$) is a ratio between the fraction of individuals susceptible per day (β) and the fraction of recoveries (γ); represented as:

$$R_\circ = \beta/\gamma$$

The value of $R_\circ$ plays a significant role in determining the infectiousness of a certain disease-causing organism. Therefore, the rate of change in infected individuals is directly dependent on the $R_\circ$, given by:

$$dI/dT = (R_\circ S/N - 1) I$$

Further assumptions of the SIR model assume that if the $R_\circ$ is greater than the ratio of total population and the susceptible cases at time zero then it would imply that the outbreak will turn into a full-fledged epidemic.

$$RR_\circ > N/(0)$$
$$dI/dt\ (0) > N/(0)$$

Similarly, if the $R_\circ$ is less than N/S (0), then it would imply that the outbreak will not cause an epidemic. Therefore, the $R_\circ$ plays a crucial role in determining the fate of an epidemic.

$$R_\circ < N/(0)$$
$$dI/dt\ (0) < N/(0)$$

Model Parameters: In the case of COVID-19, the value of $R_\circ$ is highly variable and varies from country to country. Several sources report a range of $R_\circ$ values between 1.4–3.9, therefore, we took an average value of 2.65 for our current analysis. The value of $R_\circ$ will continue to evolve as the epidemic progresses throughout the globe. The value of γ was considered based on the average infectious period for COVID-19, so γ=0.14. The value of β was calculated to be 0.378 from equation

$$R_\circ = \beta/\gamma$$

The so was assumed to be 12,344,408 since the entire population of Balochistan is susceptible to COVID-19, as the disease is new and is spreading across all regions.

Results

The SIR model for the spread of COVID-19 in Balochistan, under the assumptions mentioned in Model Parameters, indicate that the number of infections will peak on Day 45 (5th July 2020), where 3,000,000 individuals could be potentially infected. Over all 25% of the total population of Balochistan will be affected by this disease with 98% (i.e 2940,000) recovery rate by the end of 15th July 2020.

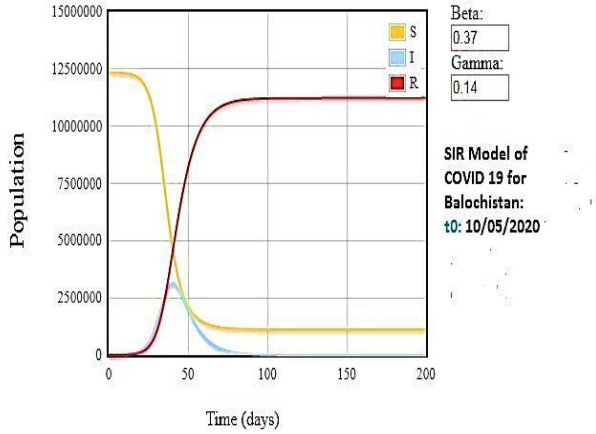

Figure 1; The SIR Model of the COVID-19 Epidemic in Balochistan. The simulations suggest that peak infection day will fall on T=45, where $I_{(45)}$ =3000000. The epidemic should have resolved by T=100 where the value of $R_{(120)}$ =2940,000. Susceptible cases (S) shown in orange, Infected cases (I) shown in light blue and Recovered cases (R) shown in Green. The x-axis represents the number of days, whereas the y-axis represents the number of cases.

Discussion

Our study was focused on modeling the COVID-19 epidemic in Balochistan in order to estimate the number of infections, the peak infection day, the rate of increase of infections per day and the resolution of the end-point of the epidemic. (1)

The simulation parameters were adjusted according to the population of Balochistan. Our model simulated the conditions where COVID-19 is spreading in a closed population of 12,344,408 people, without the effect of any extraneous variables such as social distancing, hand washing or travel restrictions. The values of $R_\circ$=2.65, β=0.378 and γ=0.14 were used.

According to the simulations the peak infection day will occur on 5th July 2020, where 30,00000 persons could get infected with the virus. Previous reports from China (8) have indicated that COVID-19 initially follows an exponential growth pattern (9)

coupled with asymptomatic carriers (10), leads to a rapid increase in the number of infections.

The study starts from the 10th May 2020 using the situation report and prior to 200 days the peak is predicted to have reached with 30,00000 individuals infected that is almost 25% of the population will be infected till 5th of July 2020 (11).

However, the major concern for Balochistan would be the healthcare system which would not be able to cope with the overwhelming number of patients if the trajectory remains the same. Studies place the mortality rate of COVID-19 at 2.3%, severe cases at 14% and critical cases at 5% (8, 12), which would imply that potentially 60,000 could die; 420,000 cases could become severe and 150,000 could become critical during the aftermath of epidemic in Balochistan. Therefore, there is an urgent need to implement effective measures to curb the rise in COVID-19 infections in Balochistan, otherwise it could lead to drastic consequences.

Conclusion

Estimating the true picture of COVID-19 is essential. It could help the Government of Balochistan in decision making and policy guidelines. Moreover, it would tell us the rate of spread and its potential of transfer from human to human. COVID-19 is a new disease not much is known about it and it is expected become endemic in Pakistan soon as a result, annual morbidity and mortality is expected. As the diseases can spread quickly in a population, due to its R_0 ranging in between 2 and 4 and with almost 2% mortality rate.

Conflict of interest: Authors do not have any conflict of interest to declare.

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Human/Animal Rights: No human or animal rights are violated during this study.

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Mortality Analysis of COVID-19 Confirmed Cases in Pakistan

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Significance:
We inferred a link in older age group with prevalent co-morbidities and risk of dying of COVID-19. Our findings suggested strict but tailored quarantine and isolation policies for elderly population given that he lockdown measures are already in place. We also suggest special focus on thickly populated provinces and regions showing high mortality in terms of lockdown and restriction on social activities.

ABSTRACT

Introduction: COVID-19, a novel disease, appeared in December 2019 in China and rapidly spread across the world. Till the second week of April 2020, high incidence (2.9/100,000) and cases fatality rates (1.7%) were observed in Pakistan. This study was conducted to determine the temporal and spatial distribution of the first 100 deaths attributed to COVID-19 in Pakistan and their associated demographic factors.

Method: A record review of the first 100 deaths reported among RT-PCR confirmed COVID-19 cases was conducted. Demographic, epidemiological, and risk factors information was obtained associated comorbidities and clinical signs and symptoms were recorded and frequencies were determined.

Results: A total of 100 mortalities with an overall case fatality rate of 1.67% (CFR) were analyzed. The median age of patients was 64.5 years (IQR: 54-70) with 75% (n=75) males. Among all deaths reported, 71 (71%) cases had one or more documented comorbidities at the time of diagnosis. The most frequently reported co-morbidities were: hypertension (67%), followed by Diabetes Mellitus (45%) and Ischemic Heart Diseases (27%). The most frequent presenting symptoms were shortness of breath (87%) and fever (79%). The median duration of illness was eight days (IQR: 4-11 days), the median delay reaching hospital to seek health care was three days (IQR: 0-6 days) while the median duration of hospital stay was also three days (IQR: 1-7 days). Among all, 62% had no history of international travel. The most affected age group was 60-69 years while no death reported in the age group below 20 years.

Conclusion: High CFR among old age group and its association with co-morbidities (chronic disease) suggests targeted interventions such as social distancing and strict quarantine measures for elderly and morbid people. Comparative studies among deaths and recovered patients are recommended to explore further disease dynamics.

Introduction

In December 2019, several cases of pneumonia of unknown causes were reported from Hubei, China later named as severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2). The international Committee on Taxonomy of Viruses renamed the virus as acute respiratory syndrome coronoavirus-2 (SARS-CoV-2).(1) The World Health Organization (WHO) announced the epidemic caused by SARS-CoV-2 as coronavirus disease 2019 (COVID-19). In subsequent days, world has seen a rapid spread across international borders and high rates of morbidity and mortality. (2) Considerable efforts has been made to understand the mechanism of disease arose as severe respiratory disease with 89.1% nucleotide similarity to a group of SARS-like coronavirus found in bats in China (3). Many developed countries with strong health infrastructure are facing high mortality hit. Case Fatality estimation has suggested a range of 0.25%-3.0% with highest 3.5 in China alone at its earliest(4). However, a correct estimation of the disease is still needed as the situation is changing rapidly. Some researcher suggested an unadjusted range of 4.4% to 4.8% considering rest an underestimation(5). Initial estimates among Novel Corona Infected Pneumonia (NCIP) suggested a human to human spread in symptomatic as well as asymptomatic(6). No significant difference in viral load of symptomatic and asymptomatic people (7) lead to the outcome of global spread as well as an underestimated mortality rate. (8).

Morbidity and mortality in developed countries has been documented high, attributed to having big proportion of aging population as compared to china(9). As of today, we know that virus is affecting badly the extreme ages and those with co-morbidities. (10).

Analysis of fatal cases in China has shown high rates in patients with co-morbidities of Ischemic Heart Diseases, Hypertension, and Diabetes. However, a higher risk in pregnant women has not been established so far.(11) Literature shows a death rate among hospitalized individuals was 15% with mean period of 14days from onset of symptoms to deaths of patients. (12).

Since first confirmed case reported on 26th Feb and first death reported on 12th March, 2020, number of cases are increasing exponentially and so is the case fatality rates. (13) In the light of rapidly changing epidemic situation, a rapid and ongoing epidemiological analysis of morbidities and

mortalities was pertinent for timely and robust public health responses.

Our objective was to investigate the characteristics of Patients died of novel corona disease, their spatial and temporal distribution and risk factors associated with them.

Methodology

A retrospective record review was conducted at National Institute of Health (NIH) Islamabad, to analyzed first 100 deaths reported and recorded with the National Emergency Operation Centre of NIH (NEOC), among COVID-19 cases, confirmed through RT-PCR. Demographic, epidemiological and risk factors information was obtained, and their history of travel was probed.

Overall case fatality rate was calculated, and its spatial and temporal trends were determined. Associated comorbidities and clinical signs and symptoms were recorded and their frequencies were calculated.

Study was approved by the National Institute of health's ethical review board and was exempted from written informed consent by the same. All the enrolled mortalities were diagnosed as COVID-19 positive in accordance with national guidelines using Real time PCR techniques at designated testing centres across Pakistan. Along with patients' available records review, verbal autopsies were carried out where appropriate, to gather maximum information as possible. All identifiers were removed before entering patient's data. Basic descriptive analysis was conducted using Epi Info® 7.

Results

A total of 100 mortalities (Overall CFR-1.67%) were analyzed. Incidence and mortalities showed an exponential trend over time (Fig 1).

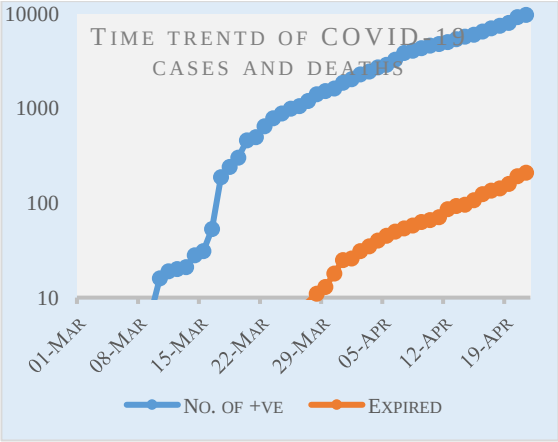

Figure 1: Incidence and mortality rates of COVID-19 in Pakistan

Median age of patients was 64.5 years with a range of 22-84years. 75% (n=75) cases were Males. Among all deaths reported 71 (71%) cases had a documented co-morbidity at the time of presentation. The most frequently reported co-morbidity among all deaths was hypertension (67%) followed by Diabetes Mellitus (45%) and Ischemic Heart Diseases (27%). First death was reported on 18th of March and most frequent presenting signs/symptoms were shortness of breath (87%) and fever (79%). Median duration of illness was eight days (range: 0-30 days), median delay in reaching to hospital was three days (range: 0-16) while median duration of hospital stay was three days (range: 0-28 days). Among all deaths reported, 62% were attributed to local transmission and had no history of international travel (table 1).

Table 1: Description of epidemiological characteristics of first 100 deaths attributed to CVID-19 in Pakistan

Characteristics	Numbers (%)
Median Age (range)	64.5 (22-84)
Male cases (%)	75 (75%)
History of documented Co-morbidity	71 (71%)
Hypertension	67/71 (94%)
Diabetes Mellitus	45/71 (63 %)
Ischemic Heart Diseases	27/71 (38%)
Tuberculosis /COPD*	3/71 (4.2%)
Others	2/71 (3%)
History of international travel	13 (13%)
History of local travel/contact with a cases	49 (49%)
No travel history	38 (38%)
Total duration of illness in days (median) (range)	8 (0-30)
Time delay in reaching hospital in days. Median (range)	3 (0-16)
Duration of hospital stay in days. Median (range)	3 (0-28)

*COPD=Chronic Obstructive Pulmonary Diseases

Among all age groups, 60-69 years were most affected while no death reported in below 20 years age groups as shown in Table 2.

Table2: Age distribution of first 100 deaths attributed to COVID-19 in Pakistan

Age groups	N (%)
20-29Y	3 (3%)
30-39Y	4 (4%)
40-49Y	6 (6%)
50-59Y	8 (8%)
60-69y	41 (41%)
70-79Y	18 (18%)
80+	10 (10%)
Total	100 (100%)

Highest case fatality rate was observed in Khyber Pakhtoonkhwa (KP) province (4.39%), while no deaths was reported from Azad Jammu and Kashmir region (fig 2)

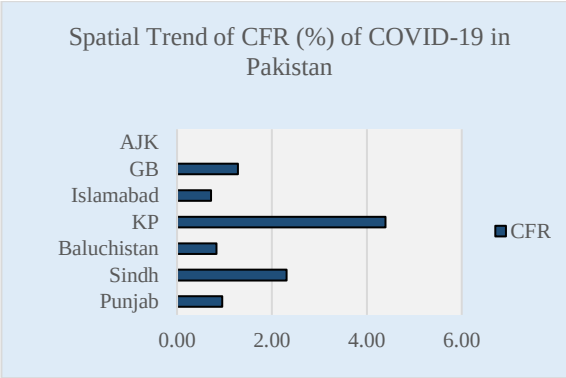

Figure 2: Geographical distribution of case fatality rate in Pakistan

Discussion

During the early phase of outbreak, reported cases were mostly travelers from other countries, mainly Iran. Testing for COVID-19 was done for symptomatic as well as asymptomatic people who had an international travel history. First death was reported on 18th March with gradual increase in CFR to 1.67% till first 100 deaths were observed, which is well below the level estimated by some researchers. (5) Initial phase of epidemic shows more cases having international travel history (14) which later on lead to local transmission. Early quarantine of travellers, prompt adoption of social distancing as well as national level lockdown policies might have played their roles in decelerating the epidemic curve. Our results showed that age above 60 years is the most vulnerable age group as depicted in other studies. (15) Children and young age groups are seemed to be protected while middle age group having highest community exposure are mildly affected. An increased CFR has been observed with increasing age. Cases presented with a range of signs and symptoms. Fever, cough, and breath shortness are the most reported signs and symptoms. However, severe acute respiratory syndrome seems the hall mark of mortality. Patients of 60 years and above presented with a rapidly progressing disease (16) along with fever, sore throat and cough as presented in other countries. (10) Patients above 60 years are dependent group of our society so are less than 12 years and usually have little community exposure as compared to rest of the population. Since results showed no death reported below 20 years age group, high CFR among 60+ patients is relatable to their low immunity and co-morbidities. Our results showed very short span of illness and even shorter duration of hospitalization overtimes. Since the prevention measures were being observed all acorns the country, access to hospital and health seeking behaviour of community played a major role in cases registration. Comorbidities like Ischemic heart diseases, diabetes and hypertension seems to play a critical role in disease progressions as determined by some other authors. (17)

Highest CFR was observed in KP province (4.39%) followed by Sindh province (2.31%). Karachi city, the most populous metropolitan and hence most affected by epidemic in Sindh province, observed early preventive measures as compared to rest of country. There is direct association between social distancing and disease transmission rate. (18) Hence a rise in CFR in KP and low in GB are directly relatable to their social distancing policies.

Conclusion

We concluded that a high fatality among elderly population and its association with co-morbidities gives us a chance to taper our intervention. Standard Operating Procedures for quarantine and isolation of elderly should be revised. Keeping our traditions and cultural norms regarding respect and care of elderly, home quarantine measures should be robust in big cities like Karachi. Male population is more prone linking their social activities in a male dominant society. Analysis of first 100 COVID-19 related deaths is a cue to assess the outcome of measures taken so far. All provinces should take all necessary measures to protect their vulnerable population to lower the CFR further down.

Limitation: Though this descriptive analysis has shown a trace of epidemiological measures, a comparative study is suggested to assess the factors associated with death as compared to recovery of the COVID-19 patients. Initial mortalities rates may vary from subsequent mortality patterns where local transmission will be high.

Ethical Considerations: Patients were not directly involved therefore informed written consent was not obtained.

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Disclosure: None

Human/Animal Rights: No human or animal rights are violated during this study.

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Factors associated with Non-adherence in Chronic Patients with Multiple Comorbid Conditions

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Significance:
Pakistan is a developing country and the frequency of people living below the poverty line is high. In non-adherence to the drug among many factors, poverty has a significant role. In recent studies, age gender and socio-economic factors have been found significantly associated with non-adherence to the prescribed therapy. In this study, it was tried to determine the association of non-adherence to the different age groups and its associated sociodemographic factors.

ABSTRACT

Background: To determine the association of non-adherence to the various age groups and related sociodemographic factors, this study was conducted.

Materials and Methods: In different departments of Services Hospital Lahore, a cross-sectional survey was conducted. 370 patients voluntarily participated in the study. The data was collected using a questionnaire. The data was analyzed using chi-square. The level of significance was 0.05%.

Results: In this study, 33.3% of patients were below the age of 40 years and 46.3% of patients were above the age of 40 years and were not adherents because of the experience that they did not get benefit from the treatment. Similarly, 21.5% of patients below age 40 and 22.3% of patients above age 40 think that they do not need medicine. 38.5% of patients below age 40 and 54.3% of patients aged above 40 stopped medicine after becoming better.

Conclusion: None-adherence found more prevalent among elderly patients.

Introduction

The US healthcare system has $170 billion of expenses annually. There is a problem of failure to adhere to drugs. Non-compliance with prescription medicines will increase the burden of healthcare services. To ensure the effectiveness of medical care regimens and more desirable health results, it is extremely important to adhere to medications. Poor medication adherence is comparatively common. (1) There are multiple studies showed that 20-30% of prescribed medications were used and 50% of medications for chronic diseases advised by physicians were not used. It is challenging to measure adherence to medicine because adherence is a single patient behaviour. Medicine failure may occur in several ways, such as a non-completion of prescribed medicine; no medications whatsoever; a lack of dose; an error; medication being taken at the wrong time of the day, without prescription (for example, with or without food) or deliberately stopping it for a while. (2) Non-adherence is defined as the *"The extent to which a person's behavior – taking medication, following a diet, and/or executing lifestyle changes, corresponds with agreed recommendations from a health care provider."* (3)

Pakistan is a developing country and the frequency of people living below the poverty line is high. In non-adherence to the drug among many factors' poverty has a significant role. In recent studies, age gender and socio-economic factors have been found significantly associated with non-adherence to the prescribed therapy. (4)

In this study, it was tried to determine the association of non-adherence to the different age groups and its associated sociodemographic factors.

Materials and Methods

It was a descriptive cross-sectional study. The study was performed at the University of Health Science (UHS), Lahore (Department of Behavioral Sciences). Data was collected from various departments of the Services Institute of Medical Sciences (SIMS). There were 370 participants included in this study. Age of 18 years without any restriction of sex, marital status, socioeconomic status, place of residence, having two or more medical conditions lasting more than three months and have been on medication for more than three months (chronic) were selected. A structured questionnaire was used to collect the data. SPSS 21.0 was used for entering and analyzing data.

Results

In this study, 370 patients with chronic diseases were selected with mean age 40.37±8.188: range of 24-64 years. 45.9% were males were and 54.1% were females. There was a ratio of 5:6 for male to female. Among the study subjects, most participants (75.40%) were enjoying family life and were married. The non-married individuals constituted a small proportion (16.8%) of the study participants.

Middle socioeconomic class individuals were present in the majority (i.e. 71.4%). Individuals belonging to higher socioeconomic classes were also present in a significant proportion (i.e. 21.6%). Individuals with hypertension reported most (i.e. n=212, 57.3%). After hypertension diabetes mellitus was the second common reported illness (i.e. n=198, 53.5%). 105 individuals (28.4%) reported with Arthritis and other joint pain-related illnesses. 101 individuals (27.3%) reported depression. 96 (25.9%) individuals were presented because of Ischemic heart disease and dyslipidemia. 81 (21.9%) individuals were presented with acid peptic disease. Total mean± SEM period of Comorbid conditions was 5.76±0.229 years among

study participants. Mean ± SEM duration of diabetes mellitus was 8.74±0.485 years and longest among other common comorbid diseases. The acid peptic disease had a mean ± SEM duration of 1.84±0.169 years which was the shortest among the most common disease conditions. Durations of other diseases are given in Table 1.

Table 1. Duration of comorbid chronic diseases

Disease	Mean (Years)	Std. Err of Mean	Std. Deviation
Diabetes mellitus	8.74	0.485	5.130
Hypertension	5.26	0.364	4.089
Asthma/COPD	5.11	0.311	2.111
Depression	2.47	0.151	1.014
Ischemic heart disease	3.35	0.342	1.531
Arthritis	3.62	0.558	2.559
Acid peptic disease	1.84	0.169	1.119
Total	5.76	0.229	4.411

Because of financial difficulties around half of the patients were unable to adhere to the prescribed regimes. Their number was 177 (47.8%).

Table 2: Treatment vs age

	40 & below	More than 40 Years	p-value
I did not get any benefit from the treatment	65(33.3%)	81(46.3%)	0.014
I did not think medicine was needed	42(21.5%)	39(22.3%)	0.900
I stopped medicine after feeling well	75(38.5%)	95(54.3%)	0.002

In this study, 33.3% of patients were below the age of 40 years and 46.3% of patients were above the age of 40 years and were not adherents because of the experience that they did not get benefit from the treatment. Similarly, 21.5% of patients below the age of 40, and 22.3% of patients above the age of 40 think that they do not need medication. 38.5% of patients were below the age of 40 and 54.3% of patients have above 40 years of age stopped taking medicine after feeling well.

Discussion

Non-adherence is strongly associated with poor health in chronic patients. This study was conducted to find a link between demographic factors and non-adherence. Non-adherence was more frequent among the participants of above 40 years of age. Factors that belong to the treatment adherence have been linked with the increasing age as per various studies published in literature[5]. The factors that were described behind this non-adherence are sociodemographic factors. Literature also suggested that old age patients are more non-persistent as compared to non-adherence. Studies have also shown that people who have undergone low-dose or standard-dose treatments that have taken several drug combinations have an increased risk of becoming non-persistent with treatment. (5)

Better adherence was documented by older patients diagnosed with chronic diseases such as hypertension, diabetes, ischemic heart disease, and chronic airway disease. (6) Similar results were reported in a recent study conducted in Kenya. Age in this study was not identified as significantly linked to non-compliance. While the prevalence of diabetes mellitus has been shown to increase with age in Kenya, the adherence to the medication showed either that the patient is not impacted by age or that the patient is improving by age. In this study, most participants were over 50 years of age and likely would live with children or members of the family. The protecting effect of these families could improve drug adhesion. In comparison, younger, professional-active patients have demonstrated greater risks of skipping their medication and non-compliance. (7)

Diabetes is estimated at 108 million in 1980 by the World Health Organization (WHO), and this number was estimated to be four-fold in 2014. The IDF estimates the world prevalence for 2000 at 151 million, for 2003 at 194 million, for 2006 at 246 million, for 2009 at 285 million, for 2011 at 366 million, for 2013 at 382 million and for 2015 at 415 million. Every estimation was based on the most recent data. (8)

Pakistan was ranked second in 21 countries in the Middle East and North Africa region by IDF diabetes atlas 2017. Statistics indicate that between 20 and 79 years of age there have been 7.5 million diabetes cases. With these figures, Pakistan has reached 18 out of 21 countries with 6.9% of the prevalence of diabetes among people aged 20 to 79. In Pakistan for the period 2016–17, the prevalence of diabetes was estimated at 27,4 million (every 20 years) cases of NDSP-II(9). According to the preliminary findings of Pakistan's 6th population and housing census in 2017 (excluding AJK and GB), there are estimates of around 100 million people residing in Pakistan, or 49% of the total 208 million. (10)

20% of people were reported to be diabetic and these individuals were of 40 years of age. Studies performed in Pakistan demonstrated 27 percent and 25 percent respectively for depression and ischemic heart disease(11).So, we could also compute that in our study diabetes mellitus and hypertension were more frequent and due to which nonadherence was more common among the elderly. Education also played an important role in treatment adherence. Those individuals who were educated they have better treatment adherence in contrast to non or less educated participants. (10)

World Health Organization (WHO) also identified various factors related to the drug adherence. WHO

identified five different variables. Among these variables are the variables related to the medical field itself, patient-related variables, various socioeconomic variables, variables related to the healthcare team, and healthcare system. (12) The explanations for non-consistency are complex and include psychosocial factors (e.g. drug usage, depression, stigma), systemic obstacles (e.g. distance from hospitals, costs for medication), linked to treatment (e.g. toxicity), and the obstacles associated with health services (e.g., lack of counseling, inadequate healthcare user experience). (13) Studies have shown that patients have little adherence to drugs and their perception of their disease.

In over 50 percent of reports, a poor understanding was reported as the explanation for non-compliance, followed by 30 percent adverse attitudes to medications and close to 15 percent cognitive impairments. Chronic disorder patients for example those with hypertension (50 percent in Pakistan) and those with hypercholesterolemia are more likely to be non-compliers. (14) Increasing therapeutic programs that do not cure conditions tends to deter patients understandably. The non-consistency ranged from 6 to 55 percent in elderly patients who are on multiple drug regimes. Patients with chronic conditions tend to stick to prescription schedules more often than once a day. Medication adherence has been correlated negatively with strong caregivers, hearing impairment, reduced cognition, and elevated medication numbers in the elderly. (15)

Conclusion

Non-adherence influenced by age, gender, socioeconomic status, and educational level of the participants. Increasing age is highly related tonon-adherence.

Conflict of interest: Authors do not have any conflict of interest to declare.

Disclosure: None

Human/Animal Rights: No human or animal rights are violated during this study.

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Doxorubicin Induced Histomorphometric Changes in the Kidney of Albino Rats and Protective Role of Nigella Sativa

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Significance:
Doxorubicin adversely affects renal tissue but owing to its remarkable therapeutic role, it cannot be substituted, hence, the strategy is to explore a remedy to combat its organ toxicity. Present study was designed accordingly to investigate the protective effect of NS against DOX related renal toxicity.

ABSTRACT

Objective: Doxorubicin is presently a leading antineoplastic drug with promising efficacy. This study was designed to investigate the histological effects of doxorubicin toxicity on rat kidneys and how much protection is provided by Nigella Sativa.

Materials & Methods: A randomized controlled trial conducted on thirty adult male wistar rats divided randomly into three equal groups. Group A served as a control. Group B was injected with weekly intraperitoneal injections of doxorubicin at a dose of 3mg/kg b.w. Group C rats received doxorubicin along with nigella sativa at a dose of 1000mg/kg b.w. orally daily. At the end of these interventions, animals were sacrificed, and kidneys were removed for the purpose of histological staining. Renal glomerular and tubules related histopathological parameters were assessed qualitatively as mild, moderate & severe. Renal glomerular diameter was digitally measured by microscope. Ethical approval was taken from Ethical Committee, Jinnah Postgraduate Medical Centre (JPMC), Karachi. All the parameters were statistically analyzed.

Results: Group B rats' renal tissue was adversely affected by the drug showing marked necrosis of tubules and the glomeruli along with interstitial cells' infiltration. Glomerular diameter was also significantly decreased in group B as compared to group A. These histological features in group C rats' renal tissue were milder and glomerular diameter was close to that of group A.

Conclusion: According to our study doxorubicin treatment proved noxious for the renal tissue, both tubules and glomeruli, while nigella sativa significantly competed against these pathological alterations.

Introduction

Adriamycin or Doxorubicin (DOX) is presently the most widely used anticancer drug in combination regimens for a wide range of neoplasia including acute lymphoblastic leukemia, and lymphomas; breast, ovarian and lung carcinomas; and pediatric malignancies like Ewing's sarcoma and neuroblastoma. (1) Its antineoplastic mechanism is tridimensional; it intercalates into DNA molecule and ceases its replication, it inhibits topoisomerase II which is an essential enzyme for DNA replication, it generates oxygen free radicals which destroy nuclear base pairs and cell membrane and lastly it binds to membrane channels and halts intercellular transport. (2) DOX was formulated by hydroxylation of daunorubicin as later was highly cardiotoxic but soon it was revealed DOX has similar toxic effects with narrow therapeutic window. DOX cannot be abandoned as it is highly effective against the cancer cells and presently there is no alternate drug. Hence, its precautionary usage is advised in case of compromised vital organs and its safe formulations are being designed and experimented. (3) Nephrotoxic effects of DOX involve renal glomeruli, renal tubules and renal interstitium and has been reported in the recent literature. (4) Its cardiotoxic effects can be countered by chelating agents but presently there is no effective remedy for the prevention of DOX induced renal toxicity. (5)

Among the hospitalized patients with acute kidney injury (AKI), drugs are responsible for 19% - 26% of cases. Older subjects and the females are more susceptible owing to their reduced body muscle. Patients with poor hepatic status (hypo-albuminemia & cirrhosis) and hypovolemic conditions are unable to metabolize the drug hence develop AKI or chronic renal failure. (6,7) In the modern era anticancer therapy is more effective than the past but concurrently the risk of nephrotoxicity is mounting and need to be addressed.

Centuries old herbs and plant derived extracts have well-documented preventive and protective role against drug induced organ toxicities. One of such plants is Nigella sativa (NS), commonly named as 'Kalonji' or 'Black Seeds,' belongs to Ranunculaceae family of kingdom plantae. It is cultivated Southwest Asia, Southern Europe, and North Africa. (8) NS is source of essential amino acids, vitamins, minerals, poly unsaturated fatty acids (linoleic acid & oleic acid) and lastly the dithymoquinone constituent which is biologically active and responsible for its pharmacological properties including antidiabetic, antihypertensive, anticancer, antioxidative, antimicrobial and anti-inflammatory properties. (9,10) NS oil is recently recommended to blend with commercial oils to reduce the peroxide value (Oxidative Level Indicator) and enhance the nutritional value. (8)

Doxorubicin adversely affects renal tissue but owing to its remarkable therapeutic role, it cannot be substituted hence the strategy is to explore a remedy to combat its organ toxicity. Present study was designed accordingly to investigate the protective effect of NS against DOX related renal toxicity.

Materials and Methods

This randomized controlled trial was conducted at Jinnah Postgraduate Medical Centre (JPMC) Karachi after approval from the Institutional Research Ethics Committee. Nigella Sativa seeds were dried and grinded to extract the powder which was stored in the refrigerator till use. Rat dose of NS was determined by

the published data. (11) DOX was obtained from Pfizer Pharma in powdered form and its sterile solution was prepared by dissolving 50gm of powder in 25ml of normal saline. (12)

30 male albino rats weighing 180–250gm and age 90-120 days were procured from Animal Care Center of JPMC Karachi and kept under optimal conditions. After two weeks of acclimatization the animals were randomly divided into three groups of 10 animals each. Group A served as a control. Group B received five weekly intraperitoneal doses of DOX at a dose of 3mg/kg body weight. (13) Group C received five weekly intraperitoneal doses of DOX at a dose of 3mg/kg body weight and aqueous suspension of powdered NS 1000mg/kg body weight orally daily for five weeks.

At the end of these interventions all the animals were sacrificed under chloroform anesthesia and the kidneys were removed from each animal which were fixed in 10% formalin for 72 hours and about 5mm thick tissue pieces were placed in separate tissue cassettes for processing in automatic tissue processor. Paraffin blocks were prepared and 4µm thick sections were cut through rotatory microtome and placed over albumenized slides. After air drying slides were stained through hematoxylin and eosin (H&E) and Periodic acid Schiff (PAS) stains according to the instructions given in literature. (14)

For calculating mean diameter of the group, five fields from each of the ten slides were observed from each animal. Diameter of three oval glomeruli per field was digitally recorded through Nikon Eclipse 50i microscope. Qualitative parameters include necrosis of glomeruli and tubules, loss of brush border, tubular vacuolations and tubular cast. Three random non-overlapping microscopic areas of a slide were selected for recording the pathological findings of each animal's kidney.

The severity of these findings was graded semi-quantitatively as: Score 0 (normal)for no pathological finding; Score + (mild) for 10% to 25% of the examined fields with histological alterations; Score ++ (moderate) for 25% to 50% of the examined fields with histological alterations and Score +++ (severe)for more than 50% of the examined fields with histological alterations. (15)

Ethical approval was taken from Ethical Committee, Jinnah Postgraduate Medical Centre (JPMC), Karachi. Data was analyzed by using SPSS (Statistical package for social sciences) software version 21. Mean & standard deviation was calculated for quantitative parameter and for comparison ANOVA and Post hoc tukey's was applied. Frequency & percentages were calculated for qualitative variables and for comparison chi square test or fisher exact test was applied.

Results:

In control group A, normal renal histology of rat kidney was observed as shown in figure 2. Renal tissue of toxic group B was adversely affected by the drug (figure 3). Corticomedullary architecture was intact while renal corpuscles had widened Bowman's space, shrunken and necrosed glomeruli with irregular capillary tuft. Renal tubules were disrupted owing to significant loss of brush border, desquamation of its cells and presence of luminal cast. Nuclei of few tubular cells were condensed indicating pyknosis and cell death. Interstitium was significantly filled with inflammatory cells. When PAS stained sections were observed, Glomerular and tubular basement membranes were found to be intact. These pathological features of tissue damage were reverted in kidney sections from group C (figure 4). Renal corpuscles showed normal capillary tuft and Bowman's capsule and necrotic changes improved as compared to the toxic group B (figure 1). Proximal and distal tubules were slightly dilated, and brush border loss was less evident as compared to group B. Interstitial edema and inflammatory cells population also decreased in group C.

Mean glomerular diameter (µm) and standard deviation of group A, B & C was 71.09 ± 7.01, 49.77 ± 3.99 and 67.50 ± 8.80 respectively. According to Tukey's post hoc test the inter group differences were statistically significant (p value < 0.01).

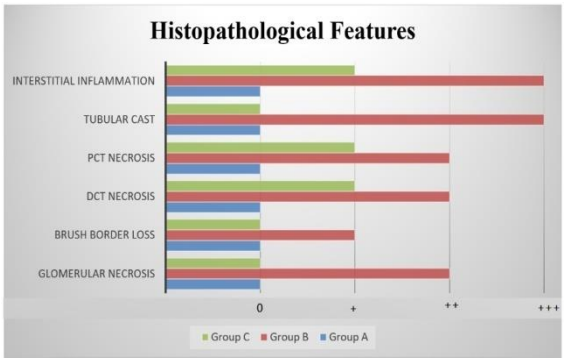

Figure 1**:** Comparison of histo-pathological features of kidney among group A, B & C.

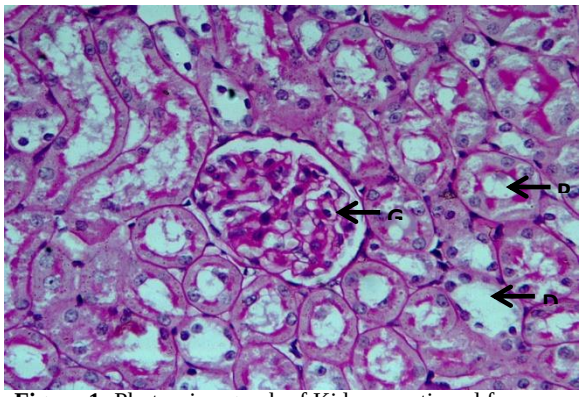

Figure 1: Photomicrograph of Kidney sectioned from Figure 2: Group A Normal Histology showing glomeruli (G), proximal tubules (P) & distal tubules (D). PAS,40X.

Discussion

NS is being prescribed in the form of grinded powder and oil for wide range of miscellaneous issues like infertility, indigestion, and traumatic brain disorders but the medics are unaware of standard dosage, formulations &pharmacological effects. (16)

Doxorubicin treated rats' kidney revealed significant glomerular necrosis evident by distorted microscopic anatomy and decreased glomerular diameter as compared to that of control group. To demonstrate DOX induced renal impairment Xie et al performed "Micro CT imaging and structural analysis" of

glomeruli and observed that number of glomeruli and their nuclei are decreased butvariation of glomerular size was different among right and left kidney. They explained DOX increases glomerular size at an early stage and vice versa at an advanced stage. (17)

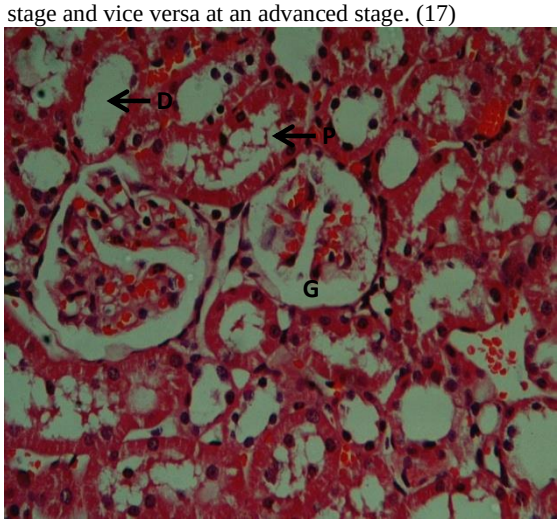

Figure 3: Photomicrograph of Kidney sectioned from toxic group B showing Proximal and distal tubules (PT & DT) with brush border loss and cellular desquamation along with a necrotic glomeruli (G). H&E, 40X.

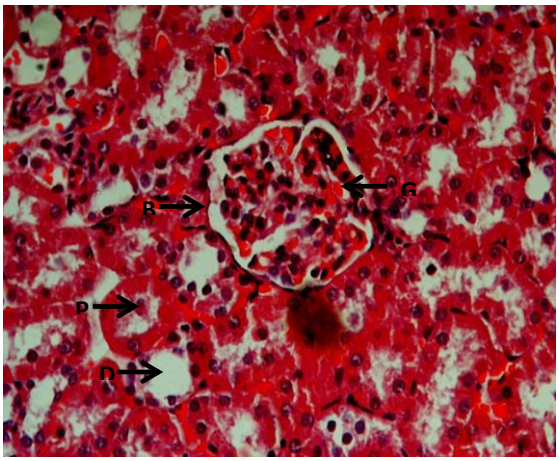

Figure 4: Photomicrograph of kidney sectioned from treatment group C, showing histological features recovery with Glomeruli (G), Bowman's capsule (BC), Proximal convoluted tubules (PCT) and Distal convoluted tubules (DCT). H&E, 40X.

DOX treatment adversely affected renal tubules both PCT and DCT. Tubules were dilated and the lumen was filled with cellular debris (cast) and desquamated cells. These pathological alterations were marked statistically significant against the control. DOX also affected the renal interstitium with significant inflammatory cells' infiltration which advocate its capability of initiating a cellular inflammatory response. (18)

Hosseinzadeh et al also observed glomerulo-tubular atrophy and inflammatory cells infiltration after DOX treatment in rats at 2.5mg/kg dose twice weekly for two weeks. Simultaneously they detected elevated inflammatory markers (TNFα- & IL-1β), elevated oxidative stress markers (malondialdehyde & nitric oxide) and lowered levels of antioxidants (catalase, superoxide dismutase and glutathione peroxide) among DOX treated animals. (19) Bilgic &Armagan also reported that single toxic dose of DOX adversely affects microscopic structure of both renal tubules and renal glomeruli and correlated these findings with biochemical markers (serum urea & creatinine) and oxidative stress. (20) Antimicrobial anticancer drugs cause acute tubular disease by direct tubular cell injury according to most recent drug induced AKI classification. (6) One possible tissue injury mechanism for these vacuolations or cellular swelling is failure of ion transport pump leading to hydrolytic changes. (21)

Microscopic findings of renal tissue specimen from group C was suggestive of substantial recovery. NS treatment prevented glomerular necrosis that was severe in the DOX intoxicated group. This finding was supported by the quantitative parameter i.e. mean glomerular diameter which was raised significantly in group C as compared to the toxic group.

NS treatment also shifted the proximal and distal tubular distortion from moderate to milder degree. Similarly, tubular cast was significantly and brush border loss was non-significantly reduced in group C. NS treatment reduced the concentration of inflammatory cells from renal interstitium that was severe with DOX intoxication which depicts its anti-inflammatory properties.

Contrary to our observations, Hadjzadeh et al., described NS effect as a nephro-protective agent is not significant as it reverted cisplatin induced histological features of glomeruli and tubules but chemical parameters were worsened. This may be because of difference of NS dose and the toxic agent. (22)

Hasan et al worked on acetaminophen induced nephrotoxicity resulting in glomerular shrinkage, tubular distortion and tubular dilatation and concluded that both aqueous and ethanolic extract of NS can normalize these pathological alterations. (23) This protection against drug toxicity is brought about by its antioxidative activity and prostaglandins' synthesis which improves renal perfusion by vasodilation. (24)

Concluding remarks of a recent meta-analysis stated that NS has definitive hepato-reno-protective role if the dose and duration of drug intake is optimal. (25) Bashandy et al., studied hepatotoxic effects of DOX and its protection by NS the end note cited that percentage change from oxidants to antioxidants was significantly higher in NS treated rats. (26)

Conclusion

Our study demonstrates that doxorubicin treatment significantly disrupts renal tubular and renal glomerular microarchitecture of rat's kidney. It also endorses recruitment of inflammatory cells throughout the renal interstium. NS treatment effectively relapsed these pathological effects and may act as a potential renoprotective agent against DOX toxicity.

Conflict of interest: Authors do not have any conflict of interest to declare.

Disclosure: None

Human/Animal Rights: No human or animal rights are violated during this study.

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Factors behind the prevalence of smoking: A case study of Mohtarma Benazir Bhutto Shaheed Medical College, Mirpur, Azad Jammu & Kashmir

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Significance:
Pakistani tobacco smokers spend 250 billion PKR on more than 64 billion cigarettes consistently. Gold Leaf, the well-known brand in Pakistan is accessible at a cost of 140 PKR for one pack of 20 cigarettes. The least expensive cigarettes accessible in the market are for 50 PKR per pack of 20 cigarettes. The foreign made and expensive cigarettes are additionally accessible in the market which can go up to 200 PKR or more per pack. Current study investigated factors behind prevalence of smoking.

ABSTRACT

Objectives: The objectives of research were to analyze the smoking behavior among the medical students and to examine the factors behind the prevalence of smoking among the students of Mohtarma Benazir Bhutto Shaheed Medical College while recommendations are made on study findings.

Materials and Methods:
Quantitative research design is used while nature of research is descriptive cross-sectional. Sample size of the study was 500 Medical Students (First year MBBS to final year MBBS). Non-probability convenience sampling technique was used to extract the sample. The data was collected through self-structured mixed questionnaire and analyzed by employing SPSS.

Results: They faced difficulty in refraining the smoking stuff which might be the educational and socio-cultural pressures which they are expected to contain in the society. The knowledge and legislation were supported by the students as legislation should be carried out to ensure the smoke free environment in College.

Conclusion: Students of Medical College Mirpur have been found addict to the smoking. However, they have been found conscious towards their smoking status while experiencing different brands.

Introduction

Tobacco addiction, nowadays, is one of the biggest health problems across the world. According to a survey conducted by World Health Organization (WHO), smoking is one of the worst habits that is spreading more rapidly all around the world. (1) Smoking has had been a risk factor for cardiovascular and respiratory diseases and Tobacco use has also been source of different types of cancer. (2) The consumption of tobacco is the main preventable cause of death in the whole world as almost 70% of the deaths occur in developing countries due to smoking. (3) It is pertinent fact reported by (WHO) that more than 600,000 lose their lives from breathing another people's smoke. In addition, smoking has been the cause of life expectancy reduction, increase in medical expenses and loss in productivity during the lifetime of a person. (4) Therefore, WHO gives priority to programs related to smoking prevention. (5, 6) On the other hand, the trend of smoking among the college students has been increased. (7, 8) However, this study is conducted to examine the prevalence and pattern of various types of smoking. (9) For the last few decades, there has been significant increase in number of college smokers. WHO has declared the act of smoking addiction as a smoking dependence syndrome in the international classification of disease. (5, 6) Cigarettes and other stuff of tobacco use are addictive. (8) The patterns of tobacco use are regular and compulsive and the withdrawal syndrome that normally accompanies abstinence occurs. This particular attitude develops among the students regardless of their gender and other characteristics. (10) These young people are using different stuff of smoking other than cigarettes pertaining even toxic substances across the world. (11) The substances used by these students might carry the socio-cultural pressures and expectations adhered by them. (12)

Different studies have revealed that frequency of smoking increases among the students when they subsequently pass through 1st year to 5th year and most addicts are found in the last year of their degree (13,4) it is pertinent here to devise any anti-smoking law or policy by the institution. Furthermore, 40% of the non-smoker students are more likely to become smokers when they enter college in their first year(1). Although, there are various reasons that promote smoking habits among the adults; one of the common factors stems from family socialization where the parents and peers are great source of maturing such practices sought at early age (7,13,4).

The smoking habit is common in students across the world as well as in Pakistan. (14, 15) According to the study, 9.7% of 7th grade students (both boys and girls) and 9th were active smokers, 24.6% had smoked at some time and 10.2% were susceptible to initiation, statistics that turned out to be higher with the passage of time. Diverse reasons were outlined by the young people, emphasized the belief so much in girls as in boys that smoking makes them appear more attractive. A study outburst that a high proportion of the respondents, 90.6%, said they were aware that cigarette smoke harms other people, while 84.3% agreed to ban smoking in colleges schools and other higher educational institutions (HEIs). (9, 15, 16).

Seemingly, smoking is a common practice at various medical colleges that lead to deaths and health issues in the world. (11) According to a study, Pakistan is amongst the high tobacco consumption countries across South Asia. (10)

Pakistani tobacco smokers spend Rs. 250 billion on more than 64 billion cigarettes consistently. (17) The cost of cigarette is considered around Rs. 4 and the aggregate cost of 64.48bn cigarettes comes to assessed Rs. 258bn roughly. (18) Gold Leaf, the well-known brand in Pakistan is accessible at a cost of Rs. 140 for every pack of 20 cigarettes (Rs. 7 for each cigarette). The least expensive cigarettes accessible in the market are Rs. 50 for each pack of 20 cigarettes or Rs 2.5 per cigarette. The foreign made and expensive cigarettes are additionally accessible in the market which can go up to Rs. 200 or more for every pack. (19) Pakistan Tobacco Company Limited is taking real part in tobacco industry of Pakistan.

Objectives: To know the smoking behavior among the medical students, to unpack the factors behind the prevalence of smoking among the students of Mohtarma Benazir Bhutto Shaheed Medical College and to make recommendations based on study finding to address the issue under study.

Materials and Methods

This research employed quantitative research design, cross-sectional technique, to assess the prevalence of smoking among the students of Mohtarma Benazir Bhutto Shaheed Medical College, Mirpur Azad Kashmir. Data collection was carried out through primary sources while data was collected through structured questionnaire. Furthermore, out of the total population 2000 of Medical College a sample size of 500 students was taken for the study. Non-probability (convenience) sampling technique was used to access the sample. Questionnaire was used to achieve the information from the respondents. The tool was designed by the researcher and the data was collected carefully. The most common procedure to explore the factors involve in this study is One Sample T-test. It gives alternative explanation of the variables which is not possible through any other technique. It is carried out through a close group in which it is used as means to establish the relative importance of independent or explanatory variables to the dependent or responsive variables. The dependent variable was taken gender while independent variables were Refrain Smoking, Monthly Expenses on Smoking, Different Stuff of Smoking, Different Brands, Hours Spent on Smoking and Smoking Status of the respondents. Against the gender, all these variables were tested while results were tabulated and interpreted. On the other hand, non-parametric tests were also employed to check the strength of association among the variables, lambda and Goodman and Kruskal tau tests were employed to check the strength and direction of association between the Banning of Smoking and Legislation for the Control of the Smoking in College. The lambda and Goodman and Kruskal tau test showed the strong association between the variables.

Results:

The above table illustrates that among the 500 selected respondents, 87 percent were found male students while 13 percent were female students who confessed that they smoke either occasionally or permanently. However, smoking behavior is found among all the participants undertaken in the study. It is therefore established from the sample undertaken in the study that students of MBBS (both male and female) Mohtarma Benazir Bhutto Shaheed Medical College, Mirpur Azad Kashmir are mainly addicted to the smoking. This evidence supports the proposition that prevalence of smoking behavior among the medical students has been at large scale and students are found addict to smoking regardless of their gender. (20, 21)

Table 2: Gender distribution of respondents

MBBS Class	Male	Female	Total
1st year	84	16	100
2nd year	87	13	100
3rd year	89	11	100
4th year	92	08	100
5th year	83	17	100
Total	435 (87%)	65 (13%)	500

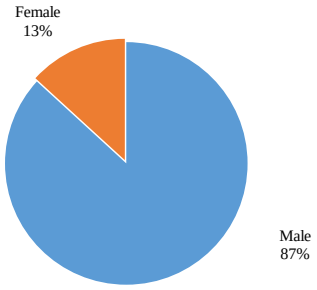

Figure 2: Gender distribution of respondents

Independent sample t test (Dependent variable is gender)

Note: all these hypotheses are approved with p-value of less than 0.05.

According to the results of One Sample T-test following illustration was derived hypotheses wise.

1. **There is significant difference of facing difficulty to refrain from smoking by male and female respondents.**
   The results were drawn that gender and difficulty faced by the students to avoid the smoking has significant relationship which denotes that gender relation with the

difficulty faced by the medical students is linked and smoking cannot be avoided easily. Results show that for smokers' gender might be the source of the avoiding the smoking in female students while it can arouse the male students to get addict of it. Based on the results, it is concluded that smoking is more likely associated with masculine or feminine character and might be an act of men (male students) to supersede women (female Students) or an act of females to avoid males and vice versa. (24) The students might believe that the fashion and company greatly influence (23) them in developing their smoking habit. (25,26).

2. **There is significant difference of monthly expenses on smoking by male and female respondents.**
   It has been observed that there is strong relationship between gender and the monthly expenses of the students. The smokers allocate a significant part of their monthly expenditures to smoking which may either increase their monthly expenses or they might find the budgetary constraints, but the relationship notifies here that gender and monthly expenses are associated with the male and female students. (27) It may be the educational pressures to contain the smoking habits while they might come across the financial issues to meet the both ends. (28)
3. **There is significant difference of smoking tobacco in other forms by male and female respondents.**
   The significant relationship has been found between the gender and different stuff of the smoking among the students. It illustrates that students among male and female have been addicted to the different smoking stuff besides smoking of the cigarettes. (29) The reason behind it may be the pressure of education as well as other socio-cultural and familial pressures. The students may find the different source of satisfaction by utilizing the different smoking stuff. (30)
4. **There is significant difference of brands of cigarette smoked by male and female respondents.**
   Here comes again the significant difference between the gender and brands of cigarettes. The interest of the male and female students may vary at large scale in making choice of the brands of cigarettes. (31) As different stuff is available in the market while male and female stuff can also make their priorities in terms of the flavors and tobacco and nicotine amount. It is therefore concluded that the brands of the cigarettes are directly proportional to the gender among the medical students because the brands are tried first and gradually it becomes the habit. (28)
5. **There is significant difference of Hours to smoke more cigarettes by male and female respondents.**
   The significant difference between gender and hours of smoking shows that smoking hours matter for both male and female students because of their gender. The hypothesis unpacked that time spent by the students on smoking is more likely associated with their gender. Likewise, male students may be more passionate to spend more time than female as the ratio of the male is higher than females. (31)
6. **There is significant difference of smoking status by male and female respondents.**
   The hypothesis reveals that the smoking status of the male and female is different. The significant values identify that male students who smoke are large in number and banded better status than the female status that have meagre ratio, but the resemblance found among medical students is evident of their difference of the status. The students might consider the cigarette as symbol of quality and recognition adopted by both men and women. (1,3)

Table 2: Decision of respondents about banning of smoking * Knowledge about legislation of smoking

Count		Knowledge about Legislation		Total
		Yes	No	
Banning of Smoking	Yes	417	33	450
	No	43	7	50
Total		460	40	500

Table 2 reveals the behavior of students about the smoking, when respondents were inquired about the banning of the smoking and knowledge about the legislation of smoking in the medical college by the authorities. A large number of students, almost 92 percent supported the process of disseminating knowledge among the students while legislation should be carried out by the authorities against smoking. (15) Only 8 percent respondents were against the spread of knowledge about the legislation of smoking. Among the 500 respondents, a large ration of 90 percent respondents agreed to ban the smoking in the campus while 10 percent didn't agree to ban on smoking like stuff. (17)

The above table illustrates the application of Lambda and Goodman and Kruskal tau test applied to the variables knowledge for the legislation and banning of

the smoking in the college premises. Lambda test denotes that there is strong association between the knowledge for the legislation and banning of the smoking. Thus, the knowledge should be disseminated on the legislation about the smoking for the medical students in the college. (21) It can only be possible when legislation will be initiated, and decision must be taken to ban the smoking in the medical college. On the other hand, Goodman and Kruskal tau also shows the strong direction of the association found between the variables taken under study. It is therefore concluded that the knowledge is needed to carry out on the legislation in order to ban the smoking in the premises of college through policy making. (1, 3, 30, 31).

Discussion

The prevalence of smoking is the worldwide issue. (1). It is equally prevalent in developed and developing countries. (3) The youth of the world is at risk due to smoking and especially the youth in schools and colleges seeking their education are involved in smoking behavior which needs to be rescued. (5) This behavior is learned either through the provided environment in the home where one or more persons might be smoker which may impact the understanding of a child to get addicted to smoking. (6) Despite this, different other factors can be the found among the youth which motivate them to adopt the smoking habits. (4) Peers and friends may also be the source of indulging into this bad habit. (7) The smoking in Pakistan is very common almost every 8/10 people smoke. (5) Among this ratio, educated people have a considerable ratio which is alarming. The people those are the source of inspiration for the youth and other sections of the society. (18) Unfortunately, they are involved in such malicious behavior. (8) On the other hand, smoking has been found spreading worldwide in young people both male and female. The recent world trends are alarming as youth is also using some other smoking stuff besides the smoking of cigarettes. (9)

In Medical College Mirpur, it is numerically found that all the students taken under study were found smokers in which 87 percent are male students while 13 percent were found female students. Furthermore, this study unpacked that the students are more likely facing the difficulty in getting out of the situation of being involved in smoking habits i.e., mainly cigarettes and other related stuff which they use to get relax and seek satisfaction. (6, 9) Another factor has been found that students have strong association between the gender and monthly expenses which clues that students might allocate an amount for the smoking like stuff and might lessen their other expenditures. (11) In this situation students might face the financial constraints to meet the other ends. There is a lot of variety of cigarettes available in the market and with the passage of time new varieties may replace the older one. Students who addicted to smoking either by trying cigar or any light stuff can be in search of changing their brands while female students can find the lighter variety to seek the satisfaction. (10,13) In addition, students spend time to the smoking was also found significant. (3) The boys can be passionate to spend more time than females in order to seek their gratification. (15) Conversely, they were found more conscious to their status of smoking which may carry different things i.e., brands and time spent to the smoking stuff. (21) Therefore, it is pertinent to mention here that medical students were found more passionate towards the smoking stuff, maintaining their status while dealing with the expenditures. (23) All the results have been found most significant showing the strength and direction of association among the variables. When asked about the knowledge and legislation for the smoking in the College premises, a large number of students, almost 92 percent supported the process of disseminating knowledge among the students while legislation should be carried out by the authorities against smoking. (10) Only 8 percent respondents were against the spread of knowledge about the legislation of smoking. Among the 500 respondents, a large ration of 90 percent respondents agreed to ban the smoking in the campus while 10 percent didn't agree to ban on smoking like stuff. (13)

Conclusion

It is thus concluded that the students of Medical College Mirpur have been found addict to the smoking. However, both male and female students were found addict to the smoking cigarettes and other smoking stuff available in the market. They have been found conscious towards their smoking status while experiencing different brands. They were found more passionate to manage the smoking hours. They faced difficulty in refraining the smoking stuff which might be the educational and socio-cultural pressures which they are expected to contain in the society. The knowledge and legislation against the smoking is important here because most of the respondents supported the dissemination of knowledge to the students from the first year while legislation should be carried out to ensure the smoke free environment in College. It is recommended that College administration must formulate the laws and develop policy to refrain the students from smoking and other stuff because these students have to cure the people when graduated. It has been found dire need of the Institution to take the radical steps to avoid the prevalence of Smoking in the College.

Conflict of interest: Authors do not have any conflict of interest to declare.

Disclosure: None

Human/Animal Rights: No human or animal rights are violated during this study.

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Traditional Uses and Pharmacological Effects of *Anagallis arvensis:* A Review

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Significance:
Anagallis arvensis has recognized medicinal values as an anti-mycotic, antimicrobial, molluscicidal, antioxidant, anti-inflammatory, anti-leishmania, antiviral, cytotoxic, and spermatogenic. The present review highlights traditional uses, phytoconstituents and pharmacological effects of Anagallis arvensis.

ABSTRACT

Anagallis arvesnsis belongs to family primulacae. It is a summer annual herb distributed worldwide or with a global spread abundantly found in Egypt, Palestine, a non-tropical region of South America, Taiwan, and India (more specifically Jammu & Kashmir). Different parts of plant contain variety of active constituents; such as glycosides, saponin, flavonoid, anthraquinone, alkaloids, rutin, kaempferol, oleananetriterpenes, anagalligenin, anagalligenone, stigasetrol, arvenin I, arvenin II, cucurbitacin B, D, E, I,L& Q, n-hexosamine, β-amyrin, sterols carbohydrates, lacceric acid. *Anagallis arvensis* has recognized medicinal values as an anti-mycotic, antimicrobial, molluscicidal, antioxidant, anti-inflammatory, anti-leishmania, antiviral, cytotoxic, and spermatogenesis. The present review will highlight the traditional uses, phytoconstituents and pharmacological effects of *Anagallis arvensis*.

Introduction

In the traditional system of medications, plants have played a vital role in the cure or prevention of different diseases. Treatments were not only limited to humans but also to animals. (1) *Anagallis arvensis* is a summer annual herb which blossoms at the end of spring. (2) It has ability to modify according to climate. (3) It is found across the Europe and dispersed worldwide because of ruderal habitat. It is abundant in Egypt, Palestine, non-tropical region of South America, and Taiwan. (4-5) The literature witnesses 1000 species of the plant grouped in 22 genera which are further divided in 5 different tribes: Primuleae, Cyclamineae, Lysimachieae, Samoleae, and Corideae. *Anagallis* belongs to the Lysimachieae tribe comprising of 28 species. (6) This genus is characterized by some distinguishing characters, such as flowering pattern is pentamerous, nectarless, polypetalous, and have a compound ovary. Petals of this genus have nyctinastic behavior, (i.e., open up in daylight but close at dusk), which leads to self-pollination. Pattern of pedicels shows the fertilized as well as unfertilized or un-pollinated flowers. This is quite an important feature as curvature in pedicels depictsa fertilized or pollinated flower, while a uniform pedicel indicates and unfertilized or unpollinated flower. (7) Various studies have shown the medicinal value of the plant, such as an expectorant, anti-bacterial, anti-diuretic, antioxidant, antimicrobial, antiviral, antifungal, mutagenic, antimutagenic, cytotoxic, anticancer, anti-leishmaniasis, liver cirrhosis, lung problems, gallstones, kidney stones, urinary infection, and dermatological activities. (8,9) Bronchicum, Sinupret, Pectosol, and Tussipect are its herbal compounds derived from roots and flowers of plants of family primulaceae. (10)

A. arvensis contains many active constituents for instance; cucurbitacin (a glycoside) and triterpenoid series of saponins are separated from the root of the plant. Similarly, kaempferol, rutin, quercitin, spinasterol (glucoside), sterol, ß-sitosterol, and stigasterol are found in flowers of the plant. Leaves are rich inoleananetriterpenes, triterpene saponins, deglucoanagallosides, analagossides A, deglucoanagallosides B, different types of fatty acids e.g., stearic acids, linoleic acids, palpitic acids, oleic acid, anagallosides A, anagallosides B, and anagallosides C. In addition to this, aerial parts of *A. arvensis* also have many constituents, in particular, arvenin I, arvenin II, cucurbitacins B, cucurbitacins D, cucurbitacins E,ß-amyrin, n-hexacosane, rutin, anagalligenin, anagalligenone, stigasterol, ß-sitosterol, laccericacid, enzyme, and carbohydrates. (10-13) Colored species of *Anagallis arvensis* contains pelargonidin, delphinidin, 3- and 3,5-glycosides of malvidin, malvidin 3- glucosides, flavonol which are discovered by Wiering and de Vlaming (14). Two glucosidic saponins are present in *Anagallis arvensis*. (15-16) Aqueous extract of *Anagallis arvensis* contains arvenin**,** tannins, triterpenoids, saponins, and flavonoids.(17) Flavones, saponins and oleananetriterpenes are found in chloroform extract of the plant.(18) Quercetin 3-glucuronide and kaempferol 3 glucuronide are flavonoid constituents which are found in abundance in ethanolic extract of *Anagallis arvensis*, however, a little quantity of some other flavonoid constituents are also present, namely, quercetin 3,7-diglucosid, quercetin 7-glucoside, kaempferol 7-glucoside, Kaempferol 3,7-diglucosid, isorhamnetin 3-glucoside, isorhamnetin 3-glucuronid and anthocyanins are malvidin 3-rhamnoside, malvidin 3-glucoside, and pelargonidin. (19) Furthermore, anthocyanins present in *Anagallis*

arvensis are malvidin 3-glucoside and pelargonidin. (15)Structural composition of antiviral saponin is (3-0-glucose (1 →1→3 or 4)– [arabinose (1 →1→ 4 or 3)]–glucose (1 → 2)-xyloside of 23-hydroxyprotoprimulagenin A). (20) Aqueous, aqueous ethanol, ethanol, chloroform and petroleum ether extracts of *Anagallis* contain functional proteins. However, chloroform extract contains flavonoids too. (21) Dihydrocucurbitacin B, cucurbitacin B**,** cucurbitacin D, cucurbitacin E, cucurbitacin I, cucurbitacin L and cucurbitacin Q are reported to be present in *Anagallis*. (22) Methanolic HCl extraction in petal cells of plant separates the flavonoids and crystalline anthocyanins which are malvidin 3-rhamnoside, malvidin, luteolin, luteolin 7 –glucoside, quercetin 3-rhamnosid, and quercetin. (23).

Traditional Uses

The significance of traditional plants towards mindfulness of individuals and populations cannot be ignored. The compound substance in plants has therapeutic importance and they deliver a vivid physiological activity on the human body, medicinal plants play a vital role in curing illness, because of the presence of secondary metabolites. (14) In Taiwan, the whole herb of *Anagallis arvensis* is used for liver complications. (24) In Italy, *Anagallis arvensis* was used in veterinary practices for curing mastitis, because of its powerful anti-inflammatory and emollient properties. Interestingly, *Anagallis arvensis* was amongst 4 plants for treating conjunctivitis. (25) Ithas a popular use for skin diseases. The plant used topically for wound healing both in humans and animals. Different types of pharmaceutical dosage forms, including ointments and infusions, where having been applied to get both local and systemic benefits from the plant. The slurry of the leaf is used for removing the leeches from cattle's nostrils. (26-28) In rural areas of Nepal, this plant is used as a piscicidal agent while the whole plant is used for the poisoning of fish, (29) Pelotaris of Bosque used ointments for healing wounds of hands after their matches. Seeds and herb used as sudorific and in rabies. (22) In India, whole plant of *Anagallis arvensis* L. is used as sedative, stimulant and antiasthmatic, and antiflatulent in cattle. (30) In Navarra, poultice, decoction, ointment or infusion of whole or aerial parts of *Anagallis arvensis* is used as an anti-hemorrhagic and antiseptic. (31) *Anagallis arvensis* (Chari saben) is enlisted in of "Plants having Anti-tussive and Expectorant activity". (32)

Pharmacological Effects

1. Antimycotic Activity

Dermatophytes are pathogens against keratinized structures of mammals, including humans (rarely, birds). Skin, hair, nails and subcutaneous tissues of the body are rich in keratin. (34) Dermatophytoses, communicable mycoses of the skin that is infected by dermatophytes. (34) Themain drawbacks of current synthetic antifungal agents are development of resistance, toxicity or mere fungistatic effects. There is need to search for a novel and natural antifungal agent which minimizes the earlier cited limitations. Medicinal plants and plant derivatives play a vital role in drug discovery and the development of a drug. (35) *Anagallis arvensis* was the most efficacious antimycotic agent amongst 22 tested plant extracts. Aqueous extract of *Anagallis arvensis* was investigated for antifungal activity against *Trichophytonmentagrophytes* (SH13, SH1, SH8), *Trichophytonviolaceum* (S5, SH32, SH38) and *Microsporumcanis* (S14, S20, and SH41), further maintained at 10ºC on SDA slants. The serial agar dilution plate technique was employed to get the fungi toxic results. Minimum Inhibitory Concentration (MIC) of aqueous extract of *A. arvensis* measured were 25, 15, 16 mg/ml and Means of mycelial percentage inhibition were 78.2±7.30%, 100±0% and 94.2±5.90% against *Trichophyton mentagrophytes, Trichophyton violaceum, Microsporumcanis* respectively. (17) *Anagallis arvensis* leaf extract prepared with sterile water showed fungi toxic potential on test specie i.e., *Colletotrichum papaya.* (16)Similarly, ethanolic extract of *A. arvensis* is potent for phytopathogenic fungus of particular genera including *Ceratocystis*, *Cytospora*, *Fomes*, and *Pestaiotiopsis*. (18)MIC of methanolic extract of *A. arvensis* is 0.31mg/ml which is the maximum inhibition against *Candida albicans*. (36)

2. Antimicrobial Activity

Methanolic extract of *Anagallis arvensis* was further evaluated for its antimicrobial properties. Antibacterial activity was determined by using standard streptomycin against four different bacteria which are *Escherichia coli, Staphylococcus aureus, Pseudomonas aeruginosa and Bacillus subtillis* with their references ATCC 11775, ATCC 12600, ATCC 9027 and ATCC 6051 respectively. The whole protocol was performed in triplicates. The minimum inhibitory concentration of one fungus and four bacteria was calculated for all extracts individually. Growth of two bacteria *E. coli* and *B. subtillis* was inhibited by the methanolic extract of *A. arvensis*. Saponins seem to have a role as antimicrobial constituent as they can cause damage to cells. (36)Significant activity was recorded for the ethanolic extract of *Anagallis arvensis* against *P. Vulgaris* which is a gram-negative bacillus.(37)

3. Molluscicidal Activity

Anagallis arvensis is considered highly active as a molluscicidal agent for schistosomiasis. Schistosomiasis is a human infection that is caused by a trematode *Schistosoma mansoni.* This trematode

produces due to poor irrigation system. The molluscicidal ability comes primarily from its allele chemicals. A demonstration was carried out in the department of parasitology lab, National Institute of Infectious Diseases, Tokyo, two intermediate species of young snails were taken, one was *Oncomelaniaquadrasii i.e* the intermediate host of *Schistosoma japonicum* and the other was *Biophalariaglabrata*, intermediate host of *Schistosoma mansoni.* Ideal standard for mulloscicide used Niclosamide, a synthetic compound was taken as a positive control. Molluscicidal constituents' *i.e* saponins which were separated by chromatographic technique. Two compounds deglucoanagalloside B and anagallosside B were reported as molluscicidal constituents from which deglucoangalloside was more active. (9, 38)

4. Antioxidant Activity

Aqueous extract of *A. arvensis* showed more prominent results. Non-linear regression method was used to calculate the free radical scavenging activity by comparing IC_{50} values. (36)

5. Anti-Inflammatory Activity

Anagallis arvensis has reported possessing anti-inflammatory activity. Indomethacin, an analgesic and anti-inflammatory drug was used as a standard against COX-1 and for COX-2 inhibition control was nimesulide which has selectivity against COX-2. Methanolic extract of *A. arvensis* showed cyclooxygenase inhibition at significant concentration and reduced the prostaglandin synthesis; however, the extract in aqueous form was only active at a concentration equal to 1mg/ml. However, indomethacin (5 µM) had the potential of minimizing the prostaglandin synthesis to the level of 42% and the same for nimesulide (200 µM) which had 47% capability of lowering the prostaglandin synthesis. Saponins and flavonoids are responsible constituents for the anti-inflammatory potential of AA. (36)

6. Antileishmania Activity

Anagallis arvensis, alcoholic extract of whole herb is effective for anti-leishmania activity (IC50 < 0.125 µg/mL, SI > 128). The assay was confirmed by using a reference of maesabalides, at the same point both reference and plant extract showed purple spot. (39)

7. Antiviral Activity

Antiviral activity of *A. arvensis* has been cited in favor of extract made with ethanol for poliovirus as well as for HSV type 1. Triterpenoid saponins (3-0-glucose (1 →1→3 or 4)– [arabinose (1 →1→ 4 or 3)]–glucose (1 → 2)-xyloside of 23-hydroxyprotoprimulagenin A) are reported to be efficacious at a minimum concentration of 4µg/ml against poliovirus and herpes simplex viruses when in vitro activity is performed. (20)

Vero cells were observed for in-vitro antiviral studies. Saponins present in *Anagallis arvensis* are responsible for antiviral properties and have broad spectra against many viruses including HSV 1 polioviruses. These phytoconstituents not only inhibit the cytopathogenesis in the host cell but also minimize the production of new viruses. Keratitis was induced in rabbits to study invivo antiviral activity of isolated saponins from *A. arvensis* against three different standard antiviral ointments, as (3% ACV) acycloguanosine, (0.24% IUdR) 5-iodo-2'-deoxyuridine and (3% Ara-A or 3% Vira-A) 9-f-n-arabinofuranosyladenine. Daily percentage of reduction in keratitis was measured. Dose of saponins greater than 7mg/g should not be applied as it may be toxic for eye treatment. The mean reduction in infection was given as the maximum reduction percentage of acycloguanosine(81.5%) had greater reduction percentage than that of *Anagallis* (7 mg/g) 44.8% and *Anagallis* (7mg/g) had more reduction percentage than adenine arabinoside as 38.9% which was further compared with a lower reduction percentage of idoxuridine *i.e.* 31.4% and finally the least reduction percentage was shown by *Anagallis* (5 mg/g) 25.7%. (41)

8. Cytotoxic Activity

Plant as a whole has been reported for its cytotoxic activity. Survival and cell death are estimated by MTT [3-(4, 5-Dimethylthiazol-2-Yl)-2, 5-Diphenyltetrazolium Bromide] and LDH [lactate dehydrogenase] assays respectively, on cell cultures of two model cell lines DHD/K12PR and PC12, from a rat. In the presence of mitochondrial enzymes in viable cells, prognostic factor for cell survival was the change of color from yellow to a purple compound named Formazan in 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT). There was a noted inverse relation i.e., PC12 cell survival was decreased as the dose of methanolic and aqueous extracts were increased. Cells of DHD / K12PROb were responsive to the methanolic form of extracts only. Cell death was checked by replacing MTT with LDH in 96 well plates for both cells. The activity of LDH for the cells that remain untreated is measured to find out the LDH spontaneously released, the methanolic extract showed far better cytotoxicity against more sensitive PC12 cells as compared to those of DHD / K12PROb cells. (27)

9. Spermatogenetic Effects

The plant is reported for semen coagulating and spermicidal activities. (42)

Conclusion

Anagallis arvensis has reputed medicinal uses as antimycotic, antimicrobial, molluscicidal, antioxidant, anti-inflammatory, antileishmania, antiviral, cytotoxic and spermatogenesis.

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Laboratory Detection of Novel Corona Virus 2019 using Polymerase Chain Reaction

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Since mid-December 2019, several cases of a pneumonia like disease (with symptoms including fever, difficulty in breathing, cough and invasive lesions on both lungs) of unknown cause have emerged in the central Chinese city of Wuhan. Chinese authorities made a preliminary determination that the causative agent is a novel coronavirus(2019-nCoV). (1) Coronaviruses are enveloped RNA viruses belonging to Coronaviridae family and the order Nidovirales. This subfamily consists of four genera alphacoronavirus, betacoronavirus, gammacoronavirus and deltacoronavirus on the basis of their phylogenetic relationships and genomic structures. These subfamilies are broadly distributed for causing infections in humans and other mammals. (2) The alphacoronaviruses and betacoronaviruses infect only mammals. The gammacoronaviruses and deltacoronaviruses infect birds, but some of them can also infect mammals. The source of betacoronavirus 2019-nCoV is still unknown, although initial cases have been linked with south Huanan seafood market. (3) Viral infections already known to produce similar symptoms are influenza, parainfluenza, Middle East respiratory syndrome (MERS-CoV) and severe acute respiratory syndrome (SARS-CoV). (4) Laboratory investigations reported raised plasma levels of L2, IL7, IL10, GSCF, IP10, MCP1, MIP1A, and TNFα in patients. (1)

WHO reports day by day telling about spread of infection over entire globe. At time of writing this report, 2019-nCoV infection in humans has been reported in Australia, France Japan, Malaysia, Nepal, Singapore, South Korea, Taiwan, Thailand and United States. (5) Pakistan, being a partner of China Silk Route, has two-way movement of citizens, is at major risk of epidemic in the country. It is, thus, important to have designed and developed diagnostic assay for confirmation of 2019-nCoV infection, if any. Authors surveyed for recent reports of 2019-nCoV and gathered significant genomic and molecular information about the virus. Data sources utilized for this purpose were GenBank, Global Initiative on Sharing All Influenza Data (GISAID) and virlogical.org.

Corman et al. reported diagnostic assay using real-time RT-PCR. Method is good to differentiate between 2019-nCoV and SARS-CoV. (6) But we used information given in by Huang et al. to develop 2019-nCoV RNA detection technique. This laboratory procedure should be performed in Biosafety level III settings. Details of assay are as following:

RNA Extraction: Laboratories can extract virus RNA using any readymade RNA miniprep kit for downstream analysis.

PCR Recipe:

Forward primer: 5′-TCAGAATGCCAATCTCCCCAAC-3′

Reverse Primer: 5′-AAAGGTCCACCCGATACATTGA-3′

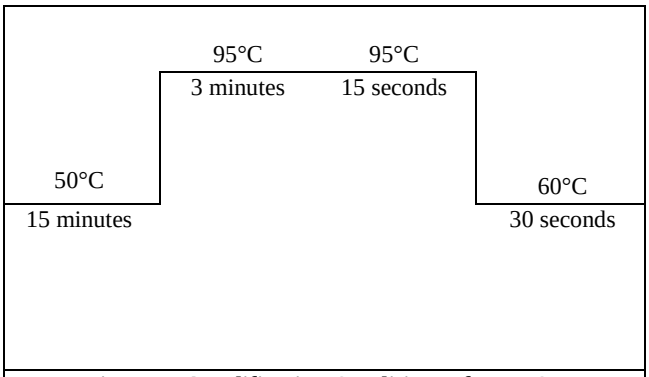

Figure 1: Amplification Conditions of RT-PCR

Mastermix: SuperScript III Platinum Sybr Green One-Step qRT-PCR Kit

Amplification conditions of PCR reaction are given in Figure 1.

Pathogen detection: Following real-time RT-PCR, presence of 2019-nCoV can be detected through real-time PCR results.

References:

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