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**Aims & Scope**

The Journal aims to publish research in all fields of clinical, diagnostic, experimental & preventive areas related to medical sciences to disseminate scholastic work among clinicians and scientists around the globe.

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# Table of Contents

# AGE REVERSAL -A NEW PARADIGM SHIFT IN MEDICAL SCIENCES

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Ageing is a physiological phenomenon in all living beings, including plants, animals and humans. It is associated with reduced physiological reserves, frailty and comorbidities, especially diabetes, cardiovascular and cerebrovascular diseases and eventual death. For a long time, ageing was considered a Deoxyribonucleic Acid (DNA) programming mechanism. However, the recent discovery by Prof. David Sinclair's team has clarified that it is an epigenetic process(1). Epigenetics is the pattern which guides DNA to work in a particular direction. There are several epigenetic mechanisms which lead to ageing, and recent research has shown that they have the potential to reverse the mechanism(1). These experiments were initially reported in yeast.

The telomere and pericentromeric are the particular regions which become more euchromatic as age advances. Telomere is proposed to be a marker of biological ageing; however, there is a lack of exact measurement cut-offs to define biological age(2). Though, there are proposed mechanisms for the determination of telomere length. Thus one potential answer to ageing is the age reversal through repair of telomere length. Another proposed process is calorie restriction, which slows down metabolism(3). Increased metabolic rate, particularly associated with a high-calorie diet, raises the production rate of toxic metabolic products such as oxidants. They raise inflammatory mechanisms and DNA mutations. All these mechanisms contribute to ageing or, at times, expedite the ageing process. Thus calorie-restricted diet improves life span by improving cellular mechanisms improving energy metabolism. There are drugs under investigation that follow the same pathways as the mechanism of a calorie-restricted diet. Such drugs include Remodelin and spermidine(3).

More recent studies have shown that each cell has a mechanism that causes the reversal of ageing if activated. Previously, Yamanaka et al. reported that the cells could return to their embryonic state by using the Yamanaka factor targeting a set of four genes(4). However, three genes were recently used to reverse cellular ageing to a younger state. This was brought about by these four genetic factors to telomere length to the original embryonic state (i.e. full length). Later, the Sinclair team used three out of four factors where the cells went to an adult younger state. The experiments have been successful in animal models being tried in monkeys now. In future, it is expected to be tested in humans. Pharmaceutical agents (i.e., Doxycycline) are under investigation to work and reverse ageing. Investigators hope to reverse diabetes, cardiovascular and cerebrovascular diseases with the same anti-ageing medication. The question is not too far from the answer.

## CONCLUSION

Age reversal is ground-breaking news in medical sciences. Since there are several diseases associated with senility, thus, the reversal of the aging concept is under investigation to treat senile diseases.

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# THE ASSESSMENT OF *TAMARIX APHYLLA* AND *CALOTROPIS PROCERA* COMPARATIVE AND COMBINE ANTIOXIDANT POTENTIAL

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**ABSTRACT**

Free radicals alter DNA, resulting in various chronic disorders, including cancer. Herbal therapy has a significant potential to block cancer progression and other chronic diseases. The *Tamarix aphylla* plays an essential role in the modulation of free radicals. *Calotropis procera* (leaves), a tropical medicinal plant, has shown protective effects against cancer progression. We have examined the antioxidant therapy of separate or combined forms of the *Tamarix aphylla* and *Calotropis procera* plant extracts. *Tamarix aphylla* demonstrated scavenging activity at various concentrations, including 100 µg/ml, 500 µg/ml, and 1000 µg/ml (29%, 37% and 62%). The scavenging activity of *Calotropis procera* at various concentrations (100 µg/ml, 500 µg/ml, and 1000 µg/ml) was 20%, 31% and 40% against the standard of ascorbic acid (65%, 77% and 84%). The mixture of both plant extracts displayed significant antioxidant potential at various concentrations 100 µg/ml, 500 µg/ml, and 1000 µg/ml which were 45%, 64% and 78%. Our study showed that the mixture of both plants has a significant antioxidant potential by comparing individual plant extracts. Further studies are recommended to elucidate the anti-cancer potential of both plant extracts mixture using in vivo approach for tumor models.

**Key Words**: *Tamarix aphylla*, *Calotropis procera*, Antioxidant activity

## INTRODUCTION

Globally cancer incidence is rising, posing a huge burden on healthcare systems. In 2019 the number of cancer patients reported from the United States of America was 1,762,450 new cases and 606,880 cancer deaths (1). Cancer is concerned with daily lifestyle using tobacco, exposure to chemicals, radiation and infectious organisms, as well as some internal factors such as inherited mutations, hormones, immune system disorders and specific random mutations (2). Oxidative stress is the inequity between producing and accumulating reactive oxygen species (ROS). The reactive oxygen species ROS is one of the main source of many diseases such as cancer, diabetes mellitus, atherosclerosis, and, more frequently gynecological diseases, especially endometriosis (3-5).

The plants are used for health benefits as a part of traditional folk medicine worldwide. To control the high percentage of various types of cancer needs new anti-cancer drugs (6). Despite the minimal risk of side effects, the possibility of medication interaction cannot be ruled out (7).

*Tamarix aphylla* belongs to the family Tamaricaceae, the most prominent Tamarix species with a height up to 18 m (60 feet). Various local names like saltcedar, Athel tree, Athel tamarisk, and Athel pine know

this plant. The plant is currently found in African and Asian countries, and local people use this plant for medicinal purposes, commonly known as tamarisk. It has been reported that *Tamarix aphylla* has strong anti-diabetic potential (8). Recent studies have shown that the *Tamarix aphylla* contains some selective secondary metabolites confirmed by the *Tamarix aphylla* phytochemical screening. The aqueous and hydroalcoholic extract of *Tamarix aphylla* of different parts confirmed that the *Tamarix aphylla* contains flavonoid glycosides, carboxylic acid steroids, cardiac glycosides, and terpenoids (9, 10). This plant has great potential to work as an anti-diabetic, antibacterial, anti-inflammatory, antifungal and in addition, it also works in periodontal disease, anti-cholinesterase and wound-healing activities. These activities are due to numerous phenolic compounds with astringent effects. In addition to traditional use, the plant has significant anti-diabetic, hypolipidemic, antifungal, antibacterial, cytotoxic, and antioxidant properties (11, 12).

*Calotropis procera* is an evergreen xerophytic plant belonging to the Apocynaceae and subfamily Asclepiadaceae. It is generally found in dry and semi-dry areas. *Calotropis procera* is a multipurpose plant widely used as a traditional medicine in North Africa, the Middle East, South Asia, and South-East Asia (13). *Calotropis procera* is generally used in society meds for treating colds, fever, uncleanliness, asthma, ailment, dermatitis, heartburn, diarrhoea, elephantiasis and skin problems (14).

Several pharmacological activities were performed for various extracts of *Calotropis procera*, like, anti-cancer, anti-diabetic, cardiovascular, anti-pyretic, anti-cancer, anti-helmintic, hypolipidemic, pain relieving, and anti-convulsant (15, 16). This study investigated the cytotoxic, antioxidant and phytotoxic effect of plants *Tamarix aphylla* extracts in combination with *Calotropis procera* and its resultant fractions

## METHODS

## CHEMICALS FOR BIOLOGICAL ACTIVITIES

2,2-diphenyl-1-picrylhydrazyl (DPPH), methanol, and aluminium foil were provided by the Department of Zoology, University of Science and Technology Bannu, Pakistan. Plants fractions and methanolic extract plants were prepared at the Laboratory of the Department of Zoology, University of Science and Technology Bannu Khyber Pakhtunkhwa, Pakistan.

## PLANT MATERIAL AND PREPARATION OF CRUDE EXTRACT

The plant extracts were collected in March 2022 from District Bannu, Khyber Pakhtunkhwa, Pakistan. Fresh, shed-dried leave of *Tamarix aphylla* and *Calotropis procera* plants were grinded into a fine powder with the help of a pestle and mortar. This powder was put into 70% methanol in such a way that the powder was completely submerged in methanol and placed at room temperature for 72 h with frequent agitation. The resulting liquid was filtered by using Whatman No. 3 filter paper. The filtrate was placed at room temperature to evaporate the liquid content. The resulting gummy methanolic extract was put into a falcon tube and lyophilized. The lyophilized sample was stored for further use.

## BIOLOGICAL ASSAYS

### Antioxidant assay

The published procedure with some modifications was followed for the assay of DPPH free radicals scavenging (17). 100 μl from each of the sample solutions of 100 μg/ml, 500 μg/ml, and 1000 μg/ml were taken. Then the 100 μl was mixed with 900 μl of DPPH solution. The exact process was repeated with 500 μl and the 1000 μl with DPPH solution. The exact process was repeated with the ascorbic acid solution. All these test tubes were incubated at 25°C for about 30 minutes in the dark because of their sensitivity toward light and checked its absorbance on a spectrophotometer at 517nm.

By using the following equation, the potential of the samples to scavenge the DPPH free radicals was calculated;

% DPPH free radicals scavenging effect = (A1-A2/A1)×100

Where A1= the absorbance of DPPH (control) and A2= the absorbance in the presence of samples.

The results were analyzed and presented in graphs.

## RESULTS

The study was designed to explore the antioxidant potential of medicinally important plant extracts such as the leaves of *Tamarix aphylla* and *Calotropis procera.*

### Antioxidant activity of *Tamarix aphylla*

The scavenging activity of the methanolic extract of *Tamarix aphylla* was analyzed in comparison with the standard ascorbic acid using DPPH free radicals assay. By increasing the extract concentration, the scavenging ability also increases, 29% at minimum concentration of 100 µg/mL while 37% and 62% with 500 µg/mL and 1000 µg/mL of *Tamarix aphylla* respectively (Figure 1).

### Antioxidant activity of *Calotropis procera*

The scavenging ability of *Calotropis procera* against free radicals DPPH shows the following different results using different concentrations at 100 µg/ml, 500 µg/ml and 1000 µg/ml. By increasing the extract concentration, the scavenging ability was also increased, which was 20% at minimum concentration while reaches up to 31% and 40% with increasing concentrations of *Calotropis procera* by comparing with control ascorbic acid scavenging activity 65,77 and 84%) as shown in Figure 2.

### Antioxidant activity of mixture of *Tamarix aphylla* and *Calotropis procera*

The combined mixture of both *Tamarix aphylla* and *Calotropis procera* in comparison with the standard ascorbic Acid was performed. The scavenging ability of DPPH and the combined extracts of *Calotropis procera* and *Tamarix aphylla* against free radicals show the following different results with different concentrations which are 100 µg/ml, 500 µg/ml and 1000 µg/ml, respectively. By increasing the extract concentration, the scavenging ability also increases i.e. 45% at minimum concentration while 64% and 78% with a maximum combined concentration of *Tamarix aphylla* and *Calotropis procera* as shown in Figure 3.
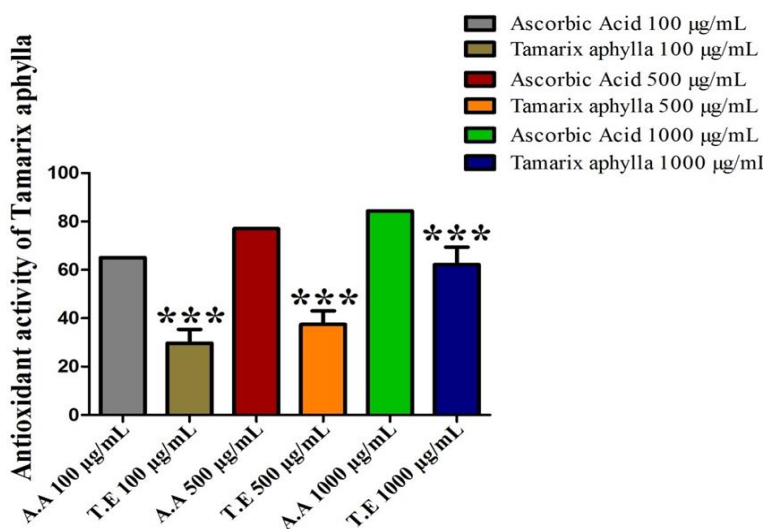


**Figure 1. Antioxidant activity of *Tamarix aphylla***
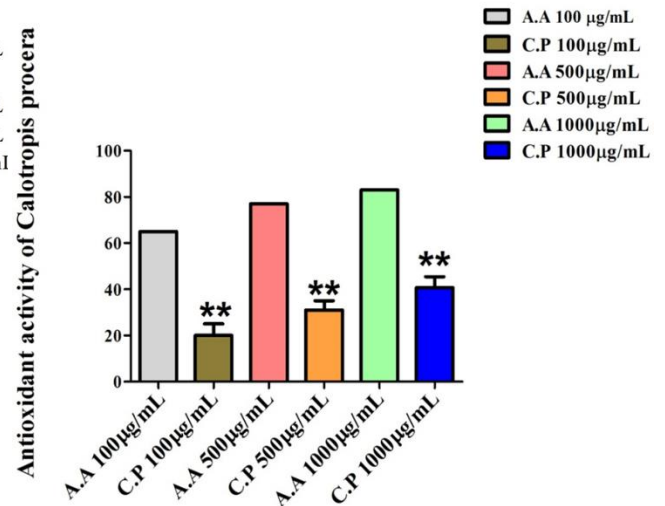
**Figure 2. Antioxidant activity of *Calotropis procera***
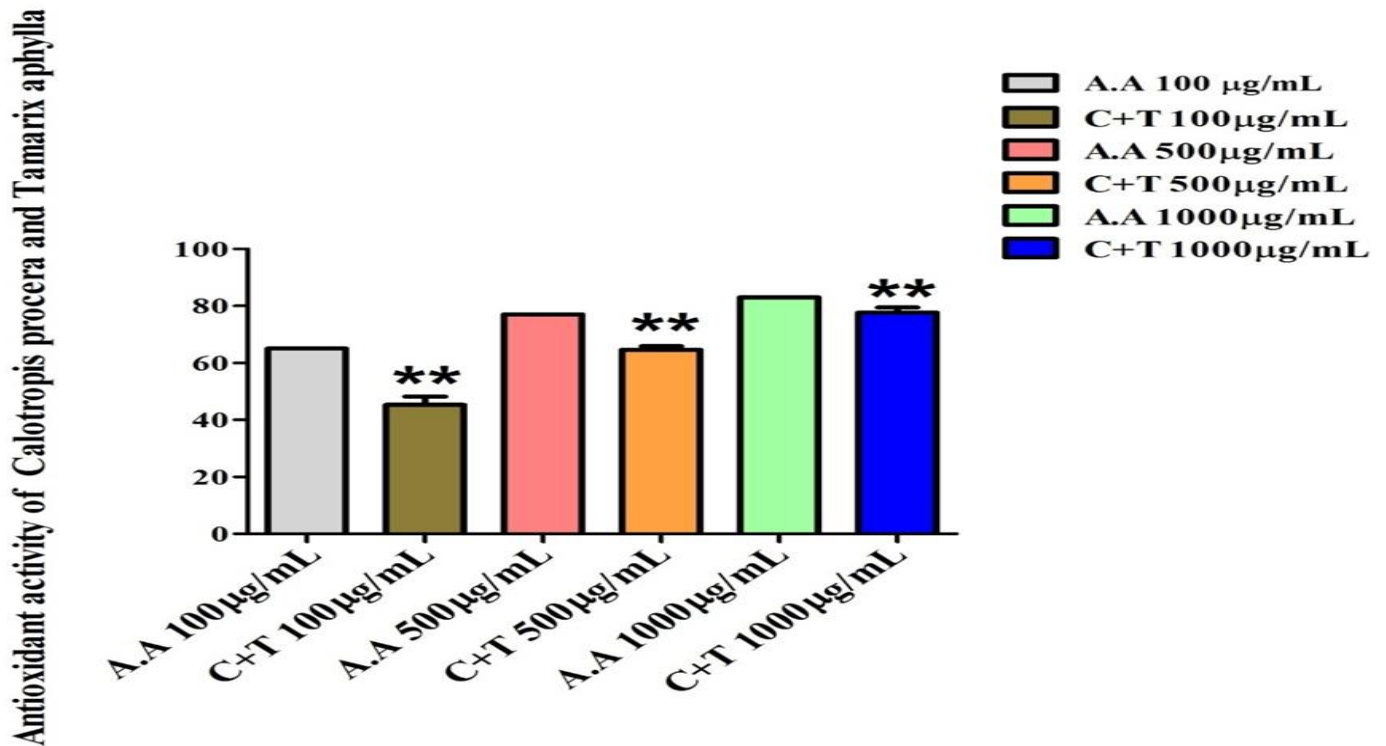
**Figure 3. Antioxidant activity of *Tamarix aphylla* and *Calotropis procera*.**

## DISCUSSION

The mutations that might result from DNA damage induced by free radicals are particularly concerning because they can impair normal cell function and possibly start cancer development. A tumor may develop when the damaged cells continue to divide and expand uncontrollably because the DNA repair mechanisms cannot correct these mutations (18, 19). The overproduced free radicals can directly react with DNA, proteins, and lipids to induce cell abnormalities (20). Free radicals, including superoxide anion, hydroxyl radicals, and hydrogen peroxide, are harmful to cellular components including DNA, lipids and proteins, and are believed to be significant contributors to many diseases such as cancer and cardiovascular diseases (21).

Natural compounds in plants can scavenge free radicals and may have anti-cancer effects. These substances also referred to as phytochemicals or phytonutrients, contain different antioxidants and other bioactive ingredients which has even been proven to reduce the risk of inflammation and illnesses such as diabetes, cardiovascular, neuro-degenerative, microbial-related diseases, and certain types of cancers (22). The findings of new anti-cancer drugs are one of the most emerging research areas of natural products. Further studies are required for the chemical characterization of the active compounds and more comprehensive biological evaluations (23). In several countries, *Tamarix aphylla* is used in traditional medicine for wounds and abscess healing, as an astringent, and for rheumatism and joint pain (24). Our previous published data elucidate that *Tamarix aphylla* has significant antioxidant potential (17). The *Tamarix aphylla* has a similar antioxidant potential to our published data. The leaves of *Calotropis procera* are used as an antidote for snake bites, rheumatic disorders, viral infection, injuries caused by burns, diarrhoea, and body pain, to cure jaundice and catarrh, antimalarial, anthelmintic and antioxidant activity (25). Next, we examined the antioxidant potential of *Calotropis procera* extracts. The obtained data

20, 31 and 40% showed less significant effects. Furthermore, the mixture of both extracts displayed considerable antioxidant potential. The mixture of both showed 45, 64 and 78% scavenging activity. We found that two combined plants had more antioxidant capability than each alone. Further research study needs to elucidate the mechanism.

## CONCLUSION

The present study suggested that the mixture of *Tamarix aphylla* and *Calotropis procera* plants extract showed significant antioxidant potential than individual extracts. Further studies using cell lines and animal models are recommended to highlight potential use of these plants for new drug development in cancer therapeutics.

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# ACUTE KIDNEY INJURY IN PATIENTS PRESENTING WITH SEVERE COVID-19 - A DESCRIPTIVE STUDY

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**ABSTRACT**

The Corona Virus Disease (COVID-19) was reported for the first time in 2019 as acute respiratory syndrome. However, its effects on other systems also became evident. Acute kidney injury (AKI) is the typical manifestation of renal involvement, reported in several cases; nevertheless, there is a lack of consensus regarding AKI manifestations of COVID-19. Therefore, this study was designed to determine the frequency of AKI in Pakistani patients presenting with severe COVID-19. It was a descriptive cross-sectional study conducted at the Department of Nephrology, Liaquat University of Medical and Health Sciences, Jamshoro, over a period of six months from 1 January 2022 to 30 June 2022. A total of 113 patients were included, who fulfilled pre-defined inclusion criteria. Acute renal injury was assessed using acute kidney injury based on the 2012 KIGDO AKI criteria. The mean age of our study's participants was 45.72 years, and of the 113 participants, 49 (43.4%) were male and 64 (56.6%) were female patients. Twenty-eight (24.8%) had diabetes, and thirty-four (30.1%) were hypertensive. 59 (52.2%) patients were found to have AKI. Age, gender, diabetes, hypertension and the severity of COVID-19 did not show any significant association with AKI. Acute kidney injury was found in a considerable number of COVID-19 patients. Therefore, close monitoring of patients must be done in all patients with regular follow-up.

**Key Words**: Acute kidney injury; COVID-19, Pneumonia Severity, Epidemiology, SARS COV-2

## INTRODUCTION

Novel Coronavirus 2019 is a member of the Human Coronavirus (HCoVs) family, which emerged in 2019 and became a global pandemic involving the whole world, including low-income nations(1). Pakistan was also not an exception to the spread of the virus (2). Although most patients have good prognosis, the elderly, patients with diabetes mellitus, cardiovascular diseases, obesity, hypertension, chronic respiratory diseases, and cancer, had the worst outcomes (3-4). Although the COVID-19 infection primarily affects the respiratory system, kidney involvement has also been observed (5). Acute kidney injury (AKI), with acute tubular necrosis (ATN) as a histo-pathological alteration, is most frequently associated kidney disease with COVID-19 infection. Sepsis, cytokine storm syndrome, hypoxia, dehydration, rhabdomyolysis, and nephrotoxic drugs are the leading causes of AKI (6-7). Mechanical ventilation is more frequently required in AKI patients(8). More than two-thirds of the AKI episodes that occurred while the patients were hospitalized reportedly started after they became critically ill(9-10).

According to Kwok Hong Chu et al., AKI complication arises in 6.7% of SARS patients, and those who develop it had high mortality, at a rate of 91.7% (11, 12). Xu et al. further confirmed and found that 39% of patients who had COVID-19 had also suffered from AKI (13). As a result, clinical approaches to preventing and managing COVID-19 patients must consider the possibility of multi-organ impairment. Prompt diagnosis and management of AKI in COVID-19 can slow its progression and help to reduce morbidity and mortality (14).

In COVID-19 patients, the development of AKI is a critical prognostic factor for survival; however, unlike other known prognostic markers, AKI may be cured with interventions. Furthermore, according to the preliminary data, the incidence of AKI in patients with COVID-19 ranged from 5% to 29%, with significant heterogeneity in different centres, presumably because of demographically diverse populations and risk factors for AKI (14-16). This may have some influence on virus variants. However, it is unclear how much COVID-19 increases the risk of AKI in a severe COVID-19 infection. According to several findings in a small number of individuals, SARS-CoV-2 may directly affect kidneys. COVID-19 showed considerable morbidity and mortality in Pakistan, but limited data is available to suggest a pattern of AKI and associated factors. Thus, this study evaluated the pattern of AKI and its association with age, gender, diabetes, hypertension and severity of COVID-19.

## METHODS

It was a descriptive cross-sectional study conducted for six months (from 1 January 2022 to 30 June 2022) at the Department of Nephrology, Liaquat University of Medical and Health Sciences, Jamshoro, Pakistan. A total of 113 patients who met inclusion criteria, such as age between 20 to 60 years, either gender and patients presenting with severe COVID-19 for more than 12 hours, were included in the study. The following criteria determined the severity of the COVID-19 patients: a positive qRT-PCR with the presence of at least one or more of the following findings:  1) Respiratory frequency > 30 breaths per minute on clinical examination; 2) SaO2 ≤ 93% on room air measured on a pulse oximeter; 3) ratio of arterial partial pressure of oxygen to fraction of inspired oxygen (PaO2/FiO2) < 300 measured on ABG; and 4) lung infiltrates on a CT scan > 50%. Patients presenting with malaria, dengue, or typhoid, and those with a history of sepsis, congestive cardiac failure, COPD, chronic kidney disease, stroke, contrast-induced nephropathy, hepatitis B, C, and HIV, and those taking nephrotoxic drugs such as aminoglycosides and NSAIDS, were excluded from the study. For sample selection, a non-probability consecutive sampling method was adopted.

This study was initiated after receiving an approval letter from the Research Ethics Committee of Liaquat University of Medical and Health Science Jamshoro (Notification No. LUMHS/REC/-245, Dated December 17, 2021). Informed written consent was taken from all enrolled patients before data collection. A brief history from the patient was taken about demographic information at the time of enrollment.

Patients were labelled with acute kidney injury based on the 2012 KIGDO AKI criteria that included any of the following: a) rise in serum creatinine of >0.3 mg/dl in 48 hours from the baseline, b) Rise in serum creatinine >1.5 times in the past seven days from the baseline c) Decrease in urine output to 0.5 ml/kg/hour for six hours by noting the urine output from the 24-hour urine output charts.

## Statistical Methods

Statistical Package for Social Sciences (SPSS Version 22) was used to analyze the data; the mean and standard deviation were calculated for continuous variables, including age and duration of severe COVID-19. The frequency and percentages of categorical variables such as gender, type II diabetes,

hypertension, and acute kidney injury (yes/no) were calculated. Age, gender, type II diabetes, duration of severe COVID-19 infection, and hypertension were stratified to determine their impact on the outcome variable. Post-stratification chi-square test was applied to correlate AKI, and a p-value of 0.05 was regarded as statistically significant.

## RESULTS

The mean age of our study population was 45.72 years, and of the 113 participants, 49 (43.4%) were male and 64 (56.6%) were female. Twenty-five (22.1%) patients were between 20-40 years, whereas 88 (77.9%) were between 41-60 years of age. Twenty-eight (24.8%) had diabetes, and 38 (30.1%) were hypertensive.

A total of 38 (33.6%) patients had severe COVID-19 for less than 24 hours, while 75 (66.4%) had severe COVID-19 for more than 24 hours. Acute kidney injury was found in 59 (52.2%) patients. Age stratification concerning AKI found that 13 (52%) patients were between the ages of 20 and 40, whereas 46 (52.3%) were between the ages of 41 and 60 (p-value =0.98, Figure 1). Gender stratification found that 46.9% of male patients, while 36 (56.2%) of females developed acute renal injury (p-value =0.32, Figure 2). Diabetes mellitus type II was found in 12 individuals (42.9%) developing AKI, which was not significantly higher than in non-diabetics (p-value = 0.25, Figure 3). A total of 17 (50%) hypertensives developed AKI, and 42 (53.2%) patients were without a history of hypertension (p-value=0.75, Figure 4). The duration of the severity of symptoms also did not show any significant influence on the development of AKI (p-value= 0.64, Figure 5).
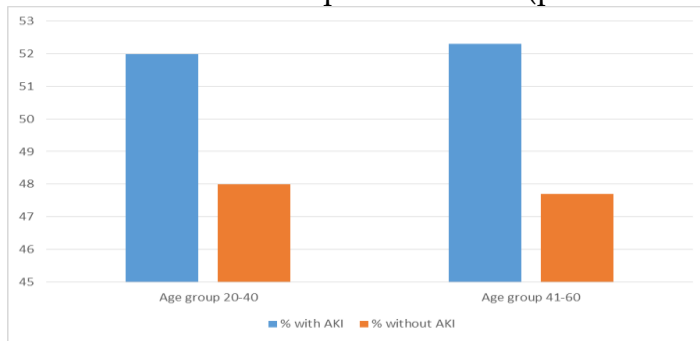


**Figure 1. Association of age with development of Acute Kidney Injury in COVID-19 patients**
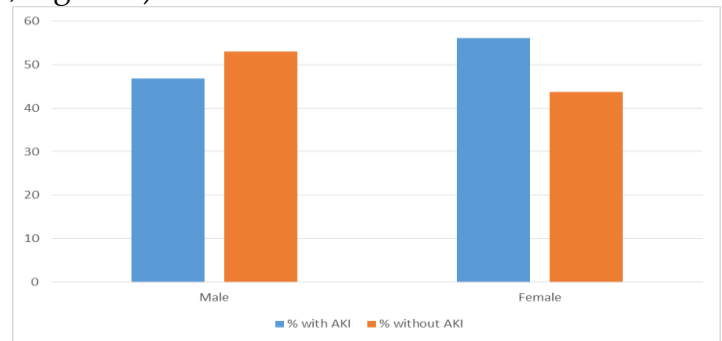


**Figure 2. Association of gender with development of Acute Kidney Injury in COVID-19 patients**
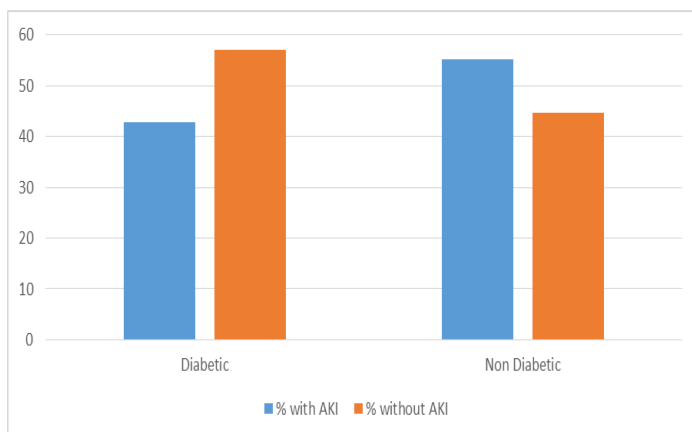


**Figure 3. Association of Diabetes Mellitus with development of Acute Kidney Injury in COVID-19 patients**
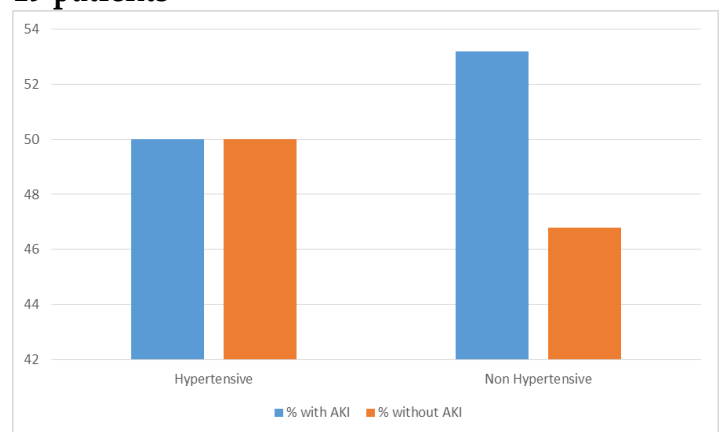


**Figure 4. Association of Hypertension with development of Acute Kidney Injury in COVID-19 patients**
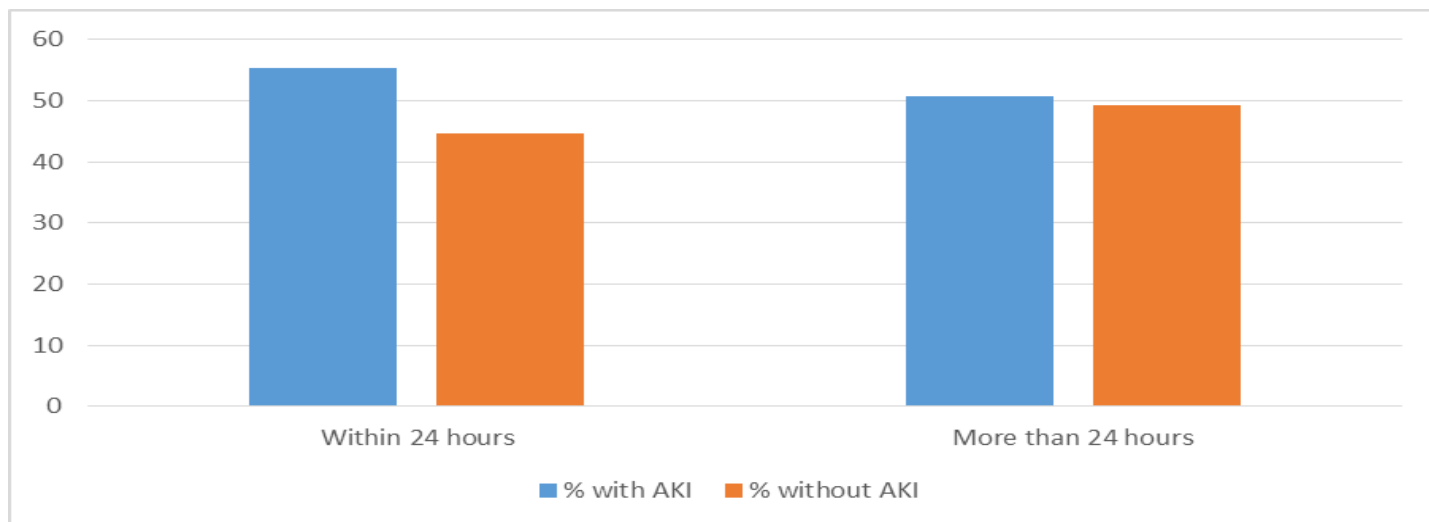
**Figure 5. Association of duration of severe symptoms with development of Acute Kidney Injury in COVID-19 patients**

## DISCUSSION

The COVID-19 infection pandemic is a multidimensional problem with far-reaching healthcare and economic consequences. The "severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)" was initially identified in Wuhan, a city in China, at the end of 2019 as a cluster of lower respiratory tract infection cases of unknown origin. Since then, the coronavirus illness pandemic has spread quickly around the world, causing the World Health Organization (WHO) to call the outbreak a global public health emergency (17-19). The clinical symptoms of SARS-CoV-2 infection appear diverse, including the majority as asymptomatic carriers of mild viral upper respiratory tract illness and severe pneumonia with respiratory failure and death. Although diffuse alveolar injury is the most prominent manifestation of COVID-19, other organ systems must also be considered. Numerous studies on the incidence of AKI in COVID-19 have reported varied rates of occurrence, which may be related to the variance in severity and baseline conditions of the patients included in the studies(20). Acute kidney Injury is unquestionably prevalent in COVID-19[20]. Of the 113 individuals included in our analysis, 59 (52.2%) developed AKI. According to Paul D. Jewell et al., 487 (39%) of the 1248 patients in the study had AKI (21). A systemic review of 60 studies by Rupesh Raina et al. found that the incidence of AKI among COVID-19 patients was 19.45%; overall patient mortality for COVID-19 was estimated to be 17.71%, whereas patient mortality for AKI was higher at 54.24%(22). In the elderly age group, diabetes and hypertension were considered as poor prognostic factors in COVID-19 patients, though they did not show any significant association with the development of AKI. Thus, AKI can be regarded as an independent factor that needs further exploration.

Kidney injury can be multifactorial, including damage caused by direct injury by the virus or the impact of the body's immune response against the virus. Also, there might be some influence of aggressive therapy in severe cases. However, these questions warrant further exploration. Our study includes patients from a single centre; the variant of COVID-19 was not assessed, which could have influenced it. The smaller sample size is considered a limitation; thus, more extensive cohort studies with the evaluation of the long-term impact of AKI on survival and overall clinical outcome are required to be done.

## CONCLUSION

A considerable number of COVID-19 patients develop acute renal injury, which is regardless of age, diabetes and hypertension, which are known as poor prognostic factors. Thus, further, more extensive cohort studies are required to explore its associated factors and long-term clinical impact.

**Ethical consideration:** This study was approved by local Research Ethics committee of Liaquat University of Medical and Health Science Jamshoro.

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**Conflict of interest:** Authors declare no conflict of Interest

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# EVALUATION OF IMPACT OF HYPERGLYCEMIA AND HYPONATREMIA ON CLINICAL OUTCOME OF ACUTE STROKE

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## ABSTRACT

Hyponatremia and hyperglycemia are common metabolic disorders which could worsen the outcome after a cerebrovascular accident (stroke). This study aimed to evaluate the impact of hyponatremia and hyperglycemia on stroke and its clinical outcome, including morbidity and mortality.

This prospective cohort study included 50 stroke patients admitted in tertiary care hospitals. Stroke severity, Glasgow coma scale (GCS), conscious level, gag reflex, clinical presentations, and outcomes were recorded. Following a stroke, patients were monitored for a period of six months, during which the patient's death was recorded on the event form. Linear logistic regression model was used to determine the stroke mortality. Hyponatremia and hyperglycaemia were associated with higher odds ratio of deaths, poor functional recovery, severe disability, low mean GCS score as compared to normonatremic and normoglycemic patients (odds ratio [OR] = 4.7; 95% CI= 0.929-43.782) and hyperglycaemia (OR= 2.74; 95% CI=0.577-13.03). Stroke patients admitted with hyperglycemia or hyponatremia were associated with greater morbidity and mortality and poor functional recovery.

**Key Words**: Stroke, hyperglycemia, hyponatremia, Morbidity, mortality

## INTRODUCTION

Cerebrovascular accident or stroke is the disruption of blood supply to the brain, which occur due to the clot formation or a hemorrhage (1). A continuous supply of blood, oxygen and glucose is required by nerves in the brain to function properly. If this supply is interrupted, brain function stops temporarily and if the interruption remains for a prolonged time, then it causes permanent brain damage. The brain controls the human body, so stroke patients could have symptoms depending on the affected part of the brain(2). Each year 130,000 Americans die due to stroke, making it fifth prominent cause of death (3). Ischemic stroke constitutes about 87% of the total reported cases of stroke (4). The risk of stroke rises with advancing age, however, there is no known youngest age limit. About 34% of patients were younger than

65years who were admitted to hospital with stroke in 2009 (5). Stroke could be caused by blocked artery (ischemic stroke) or may be due to bursting of blood vessel (haemorrhagic stroke)(5).

Hyponatremia and hyperglycemia are considered to be poor predictive elements of stroke(6, 7). In many neurological disorder i.e. meningitis, stroke, subarachnoid haemorrhage (SAH) and cerebral bleed, hyponatremia is a common electrolyte disorder(8). Hyponatremia increases mortality in patients with stroke(9). Tzoulis studied stroke patients and found a 17.3% increase in in-patient mortality rate in hyponatremic patients (10). In the prospective study carried out by Huang et al on 925 stroke patients, it was found that hyponatremic group had poor survival as compared to their normonatremic counterparts(11). Hyperglycemia is also a risk factor of stroke, as diabetic patients are more likely to suffer from cerebrovascular accidents as compared to non-diabetic population. It has negative impact on brain tissues and is linked with poor outcomes(12). A previously reported included 416 stroke patients and showed significantly higher mortality in patients who were hyperglycaemic(13). Williams et al found that 40% of 656 acute stroke patients were hyperglycemic and concluded that hyperglycemia was an important indicator in worsening the clinical outcomes after acute stroke attack(14). A number of cases are reported of cerebrovascular accidents every year in Pakistan, however, there is limited data available regarding hyponatremia and hyperglycemia in stroke. In addition most of the reported studies explored serum sodium or glycemic level separately. This study was aimed to find out the effect of hyponatremia and hyperglycemia on clinical outcome of acute stroke in terms of morbidity and mortality.

## METHODS

In this prospective cohort study, patients with primary diagnosis of stroke in emergency department of multiple public sector tertiary care hospitals based in Karachi, Pakistan were studied. Patients were diagnosed with symptoms and neuroimaging and was established by Magnetic Resonance Imaging (MRI) or else computed tomography (CT Scan). Demographic characteristics of patients such as height, patient's economic status, age, body mass index (B.M.I), gender, and weight were recorded. Moreover, patient's Glasgow coma scale (GCS), gag re-flex, conscious level, comorbidities and patient medication history were recorded.

Patients included in the study distributed in different groups accord-ing to their blood glucose and sodium levels. Groups included, normonatremic subjects with serum Na level of 135-145meq/L, hypo-natremic subjects with serum Na level less than 136 mEq/L, hypernatremia with Na level >145meq/L. Glycaemic groups were classified as normoglycemic with fasting blood glucose level (FBGL) ranging from 90 to 126 mg/dL and hyperglycemic with FBGL of more than 126 mg/dL.

After their initial stroke event, patients were subsequently monitored for a further period of six months. The consultant neurologist evaluated all subjects and related information such as con-scious level, gag reflex, GCS score, sodium and glucose blood levels were recorded. Stroke sever-ity was determined by GCS score. Death of the patient was duly recorded on the form. GCS score 13-15 was considered as mild, 9-12 as moderate and below 8 as severe (5). Hypertension was considered if the blood pressure was more than 140/90mmHg. White blood cell(WBC) count above 11,000/ mm(5) were considered as leucocytosis. Patients in whom the stroke was caused by tumour, trauma, and intraventricular haemorrhage were excluded from the study. Pregnant women and referred stroke patients were also excluded.

## Statistical Methods

Statistical package for social sciences (SPSS version 20.0) was used for data analysis. T-test was used to link the mean and Standard Deviation (±SD) of continuous variables among groups. Stroke mortality was

assessed by using liner logistic regression test method. A p-value of less than 0.05 was considered significant for hypothesis testing

## RESULTS

A total of 48 stroke patients were included in the study, where 47.9% were females, average age of subjects was 49±14year (the youngest patients was of 32years and the oldest was of 85years). Mean weight of the patients was 62±7 kg. 40 patients (83.3%) suffered from ischemic stroke. The mean random blood glucose level on admission was 162±48 (90-242). Out of total patients, 16 (33.3%) patients had hyperglycemia and 32 (66.7%) patients had normoglycemia. The mean ad-mission sodium level was 136±7 (range, 119-153). We found hyponatremia in 10 (20.8%) patients and 36 (75%) patients had normonatremia. Hypernatremia was observed in two (4.2%) stroke pa-tients.

Out of 48 patients, 10 patients (21.3%) died. An improvement was seen in 10 patients (27%), where-as 2 patients (5.4%) showed worsening in their symptoms. Hyponatremia and hyperglycaemia in-creased stroke mortality because deceased stroke patients showed low mean sodium levels (133±8) also high random serum blood glucose levels (190±39) as related to those acute stroke pa-tients who survived. Mean GCS score was lowered in deceased stroke patients as compared to survivors. (Table 1)

**Table 1. Comparison of Patient Demographic Characteristics, Clinical Outcome and Risk Factors among Survivors and Deceased Acute Stroke Patients**

| | Full sample n=48 | Survivors n=38 (78.7%) | Deceased n=10 (21.3%) |
|---|---|---|---|
| **Age (Years)** | | | |
| mean ± SD | 49±14 | 46±10 | 59±20 |
| **Gender** | | | |
| Female | 23 (47.91%) | 17 (44.70%) | 6 (60%) |
| Male | 25 (52.11%) | 21 (55.3%) | 4 (40%) |
| **Economic Status** | | | |
| Low | 27(56%) | 24 (63.1%) | 4 (40%) |
| Middle | 20(41.6%) | 13 (34.2%) | 6 (60%) |
| High | 1(2%) | 1 (2.6%) | 0 |
| **Weight (kg)** | | | |
| mean ± SD | 62±7 | 62±6.5 | 61±9 |
| **Height (cm)** | | | |
| mean ± SD | 167±9 | 168±9 | 167±10 |
| **Stroke Sub-type** | | | |
| Ischemic | 40 (83.3%) | 33 (86.8%) | 7 (70%) |
| Haemorrhagic | 8 (16.7%) | 5 (13.2%) | 3 (30%) |
| **Co-morbidities** | | | |
| Hypertension (HT) | 30 (66.7%) | 27 (71%) | 4 (40%) |
| Diabetes (DM) | 5 (11.1%) | 5 (13.1%) | 2 (20%) |
| HT and DM | 8 (17.8%) | 5 (13.1%) | 3 (30%) |
| HT and CKD | 2 (4.4%) | 1 (2.6%) | 1 (10%) |
| **Blood Pressure (BP)** | | | |
| *SBP (mm Hg) | 155±21 | 160±17 | 134.5±25 |
| *DBP (mm Hg) | 91±10 | 93±9 | 82.5±9 |

| Sodium levels mEq/L | | | |
|---|---|---|---|
| Mean ± SD | 136±6.8 | 137±6.3 | 133±8 |
| Hyponatremia | 10 (20.8%) | 5 (13.2%) | 5 (50%) |
| Normonatremia | 36 (75%) | 33 (86.8%) | 5 (50%) |
| Glucose Levels mg/dl | | | |
| *RBGL | 162±48 | 159±48 | 190±39 |
| *FBGL | 106±25 | 102±15 | 109±29 |
| Normoglycemia | 32 (66.7%) | 28 (73.6%) | 4 (40%) |
| Hyperglycemia | 16 (33.3%) | 10 (26.4%) | 6 (60%) |
| GCS | | | |
| Mean ± SD | 12±2 | 13±2 | 10±3 |
| Mild | 28 (58.3%) | 25 (65.7%) | 3 (30%) |
| Moderate | 18 (37.5%) | 13 (34.3%) | 5 (50%) |
| Severe | 2 (4.2%) | - | 2 (20%) |
| Conscious Level | | | |
| Oriented | 26 (54.2%) | 22 (57.8%) | 4 (40%) |
| Altered | 22 (45.8%) | 16 (42.2%) | 6 (60%) |

SBP= Systolic blood pressure, DBP= Diastolic blood pressure, RBGL= Random blood glucose level, FBGL= Fasting blood glucose level

In this study, normonatremia was observed in 86% stroke survivor patients and in 50% who died, whereas 73.6% patients were normoglycemic who survived acute stroke attack whereas 60% de-ceased subjects were normoglycemic. Amongst 38 survivor's patient, we have found hyponatremia in 5 patients (13.2%), hyperglycaemia in 10 (26.4%) and hypernatremia in 2 (5.4%) patients. In 10 deceased patients, hyponatremia was seen in 5 (50%) patients and hyperglycaemia in 6 (60%) patients. A summary of the data is presented in Table 2.

**Table 2. Occurrence of Blood Glucose and Sodium Concentrations in Survivors and Deceased Stroke Patients**

| | Hyponatremia (n) (%) | Normonatremia (n) (%) | Hypernatremia (n) (%) | Total (n) (%) |
|---|---|---|---|---|
| Survivors | | | | |
| Normoglycemia | 2 (5.40%) | 24 (62.10%) | 2 (5.40%) | 28 (73.6%) |
| Hyperglycemia | 3 (8.11%) | 7 (18.92%) | - | 10 (27.1%) |
| Total | 5 (13.5%) | 31 (81%) | 2 (5.4%) | 38 (100%) |
| Deceased | | | | |
| Normoglycemia | 2 (20%) | 2 (20%) | - | 4 (40%) |
| Hyperglycemia | 3 (30%) | 3 (30%) | - | 6 (60%) |
| Total | 5 (50%) | 5 (50%) | - | 10 (100%) |

## DISCUSSION

Stroke causes long-term debility and important reason of death in humans(15). Many studies have reported the relation of hyponatremia and hyperglycemia on stroke morbidity and mortality, but all included only single variable, which is either hyperglycemia or hyponatremia. The present study is distinctive in this regard, as it encompassed both hyperglycemia and hyponatremia in the same situation and finding out their influence on stroke morbidity and mortality. Linear logistic regression test is used to determine the morbidity and mortality in stroke patients. Hyponatremia and hyperglycemia are metabolic abnormalities that have negative impact in stroke patients (16) and both are considered as a threat reason of stroke(17). Kostulas et al and Rodrigues et al found that hyponatremia and hyperglycemia is related to increased stroke morality and deaths(13, 16). Various researches have shown that hyponatremia has adverse outcomes(18). In neurological patients, sodium imbalance are reported to be more common(19). Hyperglycemia is also considered as a risk factor of stroke. It has been learnt from a 15year cohort study that those patients who has diabetes, they have increased chances of ischemic stroke attack as compared to those patients who did not have diabetes(20). The patients whose blood glucose levels were more then 6.1-7.0 mm/L on admission were associated with poor functional outcomes and increased risk of 30 days mortality(21). Apoptotic ability was lower in hyperglycaemic patients as compared to normoglycemic patients. Neutrophil accumulation result due to lower apoptotic ability and increased cell proliferation. Free radical, proteolytic enzyme and other harmful substances released due to the neutrophil accumulation. This damages the blood vessels and increases cellular permeability. Damage to the blood brain barrier could also occur due to which cerebral oedema can occur(22). Patients who were hyponatremic and hyperglycemic showed lower survival. There is increased morbidity and mortality in patients who had hyponatremia and hyperglycemia when they were admitted(23). Patients who were hyponatremic or hyperglycaemic have poor gag reflex, low mean GCS score, altered conscious level and poor functional recovery as compared to normonatremic and hyperglycaemic patients. Haemorrhagic stroke was more prevalent in patients who has hyperglycaemia on admission. Higher odd of death occurred to the patients who has hyponatremia or hyperglycaemia. The limitation of the study is small sample size. The true impact of hyponatremia or hyperglycaemia on patient mortality can be determine by large sample.

## CONCLUSION

Stroke patients who were admitted with hyponatremia or hyperglycaemia, had poor clinical out-comes and were associated with increased morbidity and mortality. Improving blood glucose and sodium levels have positive outcomes in stroke patients GCS score, gag reflex and symptoms improve after correcting the glucose and sodium levels. Further large scale studies are required on the subject.

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# DETERMINATION OF ANTI-ARTHRITIC ACTIVITY OF THE LEAVES EXTRACTS OF PROSOPIS JULIFLORA (SW) DC BY USING IN VITRO METHOD

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## ABSTRACT

Rheumatoid arthritis (RA) is an autoimmune inflammatory condition with an unknown aetiology that causes cartilage and bone to erode. The ineffectiveness and side effects of the current therapeutic agents, such as glucocorticoids, disease-modifying anti-rheumatic drugs, and non-steroidal anti-inflammatory drugs (NSAIDs), highlight the need for finding new agents with more significant therapeutic potential and fewer side effects. The plant Prosopis Juliflora, also known as mesquite and a member of the Fabaceae family, has been used as a general remedy for a variety of ailments, including catarrh, diarrhoea, dysentery, wound healing, flu, measles, hoarseness, infection, and sore throat. The anti-arthritic effect of P. juliflora leaves of plant was subjected to four extraction methods: maceration, sonication, soxhalation and reflux extraction. In vitro study was conducted by using a protein denaturation assay. The IC50 values of macerated, PJE, PJE50 and PJA extracts were 355.02, 302.8, and 230.1 µg/mL, respectively. The IC50 values of the sonicated crude extracts, i.e., PJE, PJE50 and PJA, were calculated as; 3792.2, 1129.4 & 44.91 µg/mL, respectively. The IC50 values of refluxed crude extracts PJE, PJE50 and PJA were calculated as; 250.35, 337.80 & 130.36 µg/mL, respectively. The IC50 value of soxhlated crude extract PJE was determined as 160.50 µg/mL. The result shows that all the extracts possessed protein denaturation-inhibiting activity. Among all crude extracts, the PJA extract made by the sonication method is the most potent with the lowest IC50 value.

**Key Words**: Rheumatoid arthritis, Prosopis juliflora, Leaves, in vitro, anti-arthritic, protein denaturation

## INTRODUCTION

Worldwide, arthritis affects millions of people, severely limiting their ability to get on with their daily lives and contributing to musculoskeletal imbalances (1, 2). It is a term frequently used by health care professionals to describe the progressive inflammatory condition in one or more joints brought on by various factors, such as traumatic, rheumatic, and degenerative concerns that can result in muscle stiffness and restricted physical movement(3). Rheumatoid arthritis is a degenerative disease affecting people of all ages, races, gender, and geographical regions (4, 5). The patient's clinical symptoms can range from mild pain and swelling to severe forms like total or partial joint immobility, muscular

atrophy, and contractures (2). Non-steroidal anti-inflammatory drugs (NSAIDs) are typically administered to these patients as a first line of treatment as part of the medication regimen, but their prolonged use can led to some potential side effects, including gastroduodenal diseases and renal insufficiency, which are most likely caused by cyclo-oxygenase inhibition for a decrease in prostaglandin content. Due to side effects or disease progression, patients need second and even third lines of therapeutic options. Some other types of treatments available today other than NSAIDs, including corticosteroids and disease-modifying antirheumatic drugs (DMARDs), primarily focus on treating symptoms rather than the pathological causes, such as membrane stabilization, protein denaturation, etc. Additionally, using the aforementioned treatment options could result in severe liver damage and gastric bleeding(6, 7).

Therefore, researchers are looking into plants as a source of medicine to overcome all these problems and discover a safer yet equally effective therapeutic option. In our study, we have selected the plant Prosopis juliflora (SW) DC, also known as mesquite belonging to the family Fabaceae. It has been traditionally used to treat diarrhoea, catarrh, dysentery, hoarseness, measles, throat infection, and wound healing(6). It has also demonstrated antibacterial, antioxidant, antifungal, antitumor, and anthelmintic activities (8). The previous study showed that leaves of P. juliflora contain tannins, saponins, alkaloids, carbohydrates, flavonoids and cardiac glycosides(6, 9).

Thus this study was designed to identify the extraction method with the highest yield and to evaluate the protein denaturation potential of the extract as foundation work to explore its potential for the treatment of RA.

## METHODS

This was a prospective study conducted at the Department of Pharmacy, University of Sindh, Jamshoro, Pakistan between June 2022 till January 2023. Sigma Aldrich Co. in St. Louis provided all the chemicals and reagents, and all substances/solvents were of an analytical grade.

### Collection and Preparation of Extract

Leaves of P. juliflora (SW.) DC were collected from Sindh university colony, Jamshoro, Pakistan and taxonomical identification was done at the Institute of Plant Sciences, University of Sindh, Jamshoro, Pakistan (voucher no 20047). The prepared powdered leaves (15g) were extracted with water (75 ml), ethanol-water (75 ml) and ethanol (75 ml) for subjected to extraction through maceration, reflux, sonication and soxhlation. The extract was filtered and dried. The yield of obtained dried extract was calculated in % w/w.

### Effect of Protein Denaturation (egg albumin denaturation assay)

In vitro effects were checked by using a mixture (5 ml) was used, which contained 0.2 ml of egg albumin, 2.8 ml of phosphate-buffered saline (PBS) with a pH of 6.4, and 2 ml of plant extract in different concentrations (7.5, 30, 120, and 480 ug/mL). A comparable volume of PBS and egg albumin was combined for the control. The mixture was then heated for 5 minutes at 70 °C after 15 minutes of incubation at 37 °C. Their absorbance was measured at 660 nm after cooling, using the blank as a reference(10).

The percentage of inhibition of protein denaturation was calculated by using the following formula;
% inhibition= Abs control - Abs treated /Abs control ×100

## RESULTS

The soxhlation method showed the highest yield at 22.3% using ethanolic PJE, while reflux extraction showed the highest yield in aqueous PJA at 26.8%. Table 1 shows the percentage yield of P. juliflora crude extracts using different methods.

### In vitro anti-arthritic effect of P. juliflora through macerated extracts

The macerated PJE, PJE50, and PJA extracts were used to study the in vitro impact through protein denaturation assay. All extracts lowered protein denaturation in a dose-dependent and substantial way, but PJA appears to be the most potent with the lowest IC50 value (230.1 ± 13.6µg/ml). Figure 1 presents a summary of the in vitro activity of all extracts.



| Extracts | IC$_{50}$ ± S.D (µg/mL) |
|----------|--------------------------|
| PJA      | 230.1 ± 13.6             |
| PJ50     | 302.8 ± 15.7             |
| PJE      | 355.02 ± 57.04           |
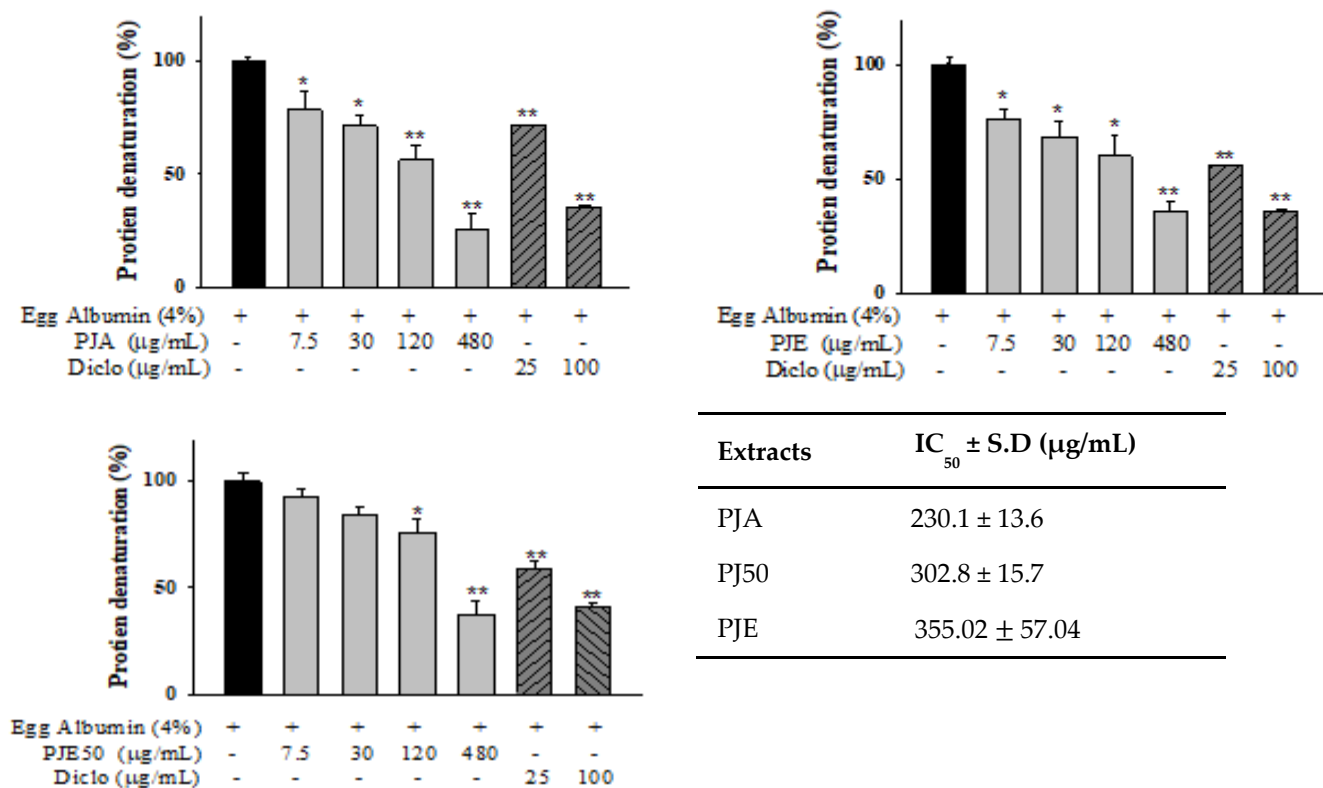
*The data is shown as mean S.D. (n=3). Paired t-test was used to examine the data's significance. Compared to the control group, \*p0.05; \*\*p0.01. PJE = ethanolic extract of P.juliflora; PJE50 = hydroalcoholic extract of P.juliflora; AfA = aqueous extract of P.juliflora; IC50 = inhibitory concentration of 50%; S.D = standard deviation*

**Figure 1: Protein denaturation inhibition of extracts of P. juliflora made by maceration**

### In vitro anti-arthritic effect of P. juliflora through reflux extraction

The refluxed PJE, PJE50, and PJA extracts were used to study in vitro impact through protein denaturation assay. Figure 2, demonstrates that all extracts lowered protein denaturation in a dose-dependent and substantial way, but among all extracts, PJA is most potent with the lowest IC50 value (130.36 ± 4.06 µg/ml).

### In vitro anti-arthritic effect of p. juliflora through sonication

Using sonication method, the PJE, PJE50, and PJA extracts were used to study in vitro impact through protein denaturation assay. Figure 3, demonstrates that all extracts lowered protein

denaturation in a dose-dependent and significant way, but among all extracts, PJA is most potent with the lowest IC50 value (44.91 ±15.69 µg/ml).
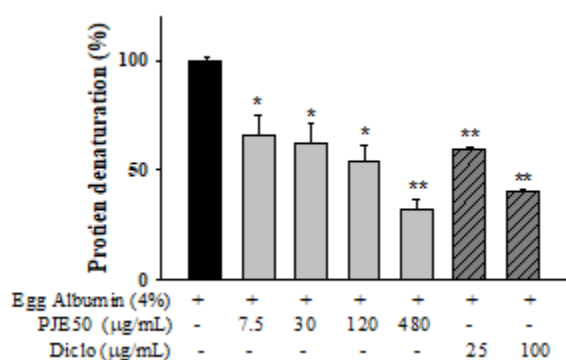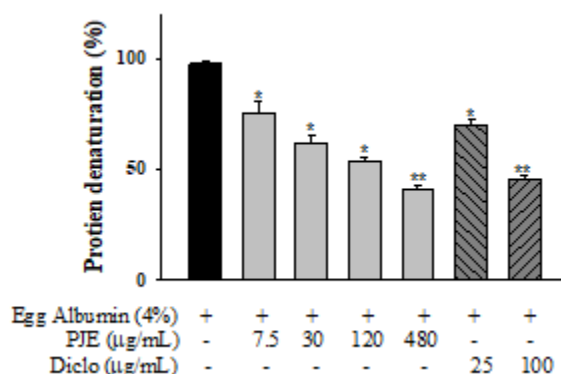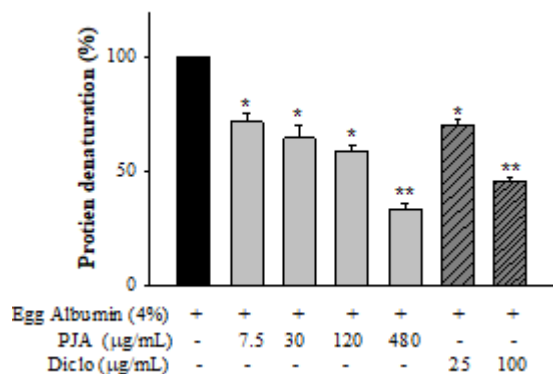


| Extracts | IC$_{50}$ ± S.D (µg/mL) |
| --- | --- |
| PJA | 130.36 ± 4.06 |
| PJ50 | 337.80 ± 22.25 |
| PJE | 250.35 ± 3.90 |

*The data were expressed as mean S.D. (n=3). A pairwise t-test was used to examine the data's significance. Compared to the control group, \*p0.05; \*\*p0.01. PJE stands for P. Juliflora ethanolic extract, PJE50 for P.juliflora hydro alcoholic extract, PJA stands for P.juliflora aqueous extract, IC50 for 50% inhibition, and S.D for standard deviation*

**Figure 2: Protein denaturation inhibition of extracts of P. juliflora made by using the reflux method**
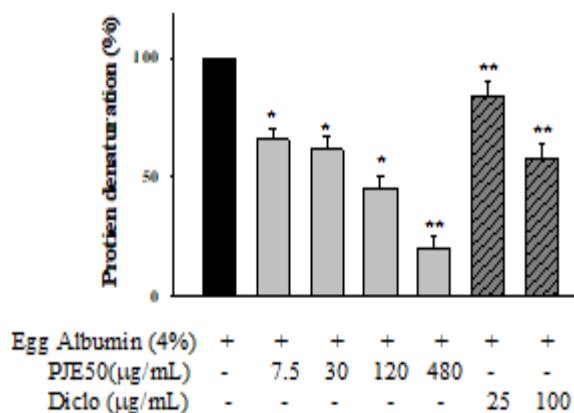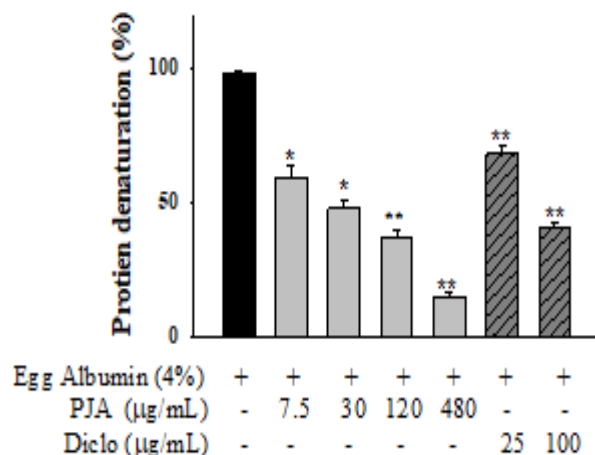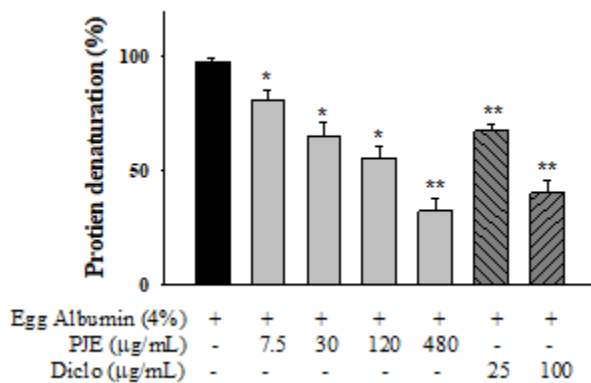
| Extracts | IC$_{50}$ ± S.D (μg/mL) |
|---|---|
| PJA | 44.91 ±15.69 |
| PJ50 | 1129.47 ± 28.37 |
| PJE | 3792.13 ± 96.92 |

*The data is expressed as mean S.D. (n=3). Paired t-test was used to examine the data's significance. Compared to the control group, \*p0.05; \*\*p0.01. PJE stands for P.juliflora ethanolic extract, PJE50 stands for P.juliflora hydroalcoholic extract, and PJA stands for P.juliflora for aqueous extract.*

**Figure 3: Protein denaturation inhibition of extracts of prosopis juliflora made by using sonication method**

## In vitro anti-arthritic effect of p. juliflora through soxhlation

Soxhlation extract of the plant also shows protein denaturation inhibition in dose-dependent and significant way(160.50 ± 16.89 μg/ml). Figure 4 presents a comparison of different doses.
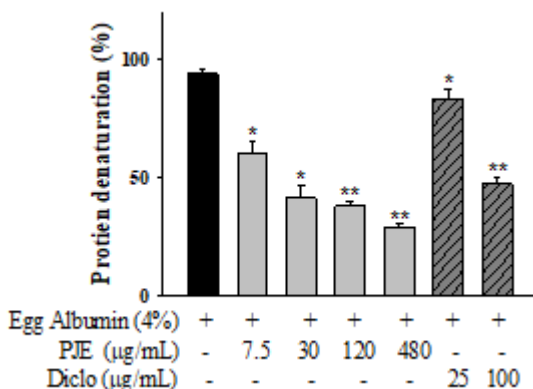


| Extract | IC$_{50}$ ± S.D (μg/mL) |
|---|---|
| PJE | 160.50 ± 16.89 |

*The data is expressed as mean S.D. (n=3). Paired t-test was used to examine the data's significance. Compared to the control group, \*p0.05; \*\*p0.01. PJE stands for P. juliflora ethanolic extract, IC50 for 50% inhibition, and S.D for standard deviation*

**Figure 4: Protein denaturation inhibition of extract of P. juliflora made by using soxhlation method**

## DISCUSSION

Rheumatoid Arthritis is a chronic illness that affects both adults and elderly people equally. Even though the prevalence rate of arthritis ranges from 0.3% to 1%, elderly women are predominantly affected. Low to middle-income countries show high rates of arthritis. Most therapeutic options, such as NSAIDs, Glucocorticoids, DMARDS and certain biological agents, demonstrate several side effects (4, 11). Even with highly harmful drug side effects, these drugs target the symptoms, but the root cause of the disease remains untreated, whereas surgical treatments can result in post-operative

complications. Prosopis juliflora is part of the family Fabaceae. It has been used traditionally for treating diarrhoea, catarrh, dysentery, hoarseness, measles, throat infection, and wound healing(12). It has also demonstrated antibacterial, antioxidant, antifungal, antitumor, and anthelmintic activities (5), but in vitro, anti-arthritic effect was not studied. The study shows that different crude leaves extract of the plant possesses potent anti -arthritic effects(13). Significant protein denaturation inhibition was determined through in vitro egg albumin denaturation assay. Among all crude extracts, aqueous extract by sonication method was found to be the most effective compared to ethanolic and hydroalcoholic extracts of this plant.

The plant has great potential to be used in novel drug development. Several plants are used for drug development of plant-based drugs. The plant extracts are natural compounds with relatively less side effects than synthetic molecules. The next line in our experiment is to test these extracts in cell lines and animal models so that these molecules can be taken to the next level of testing in the human body. This study used standard methods for extraction and analysis and showed promising results. However, not testing these molecules in animal models is considered a limitation.

## CONCLUSION

The current study proved that PJA extract of plant possesses potent anti-arthritic activity as determined by in vitro experimental models. Therefore, aqueous plant extract (sonication) may be considered for further determination of anti-arthritic effect of this plant by using in vivo studies. Further studies on animal models and cell lines are recommended.

### Conflict of interest:

All the authors declared no conflict of interest.

### Funding

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# EVALUATION OF ASTHMA: AGGRAVATING FACTORS AND FAMILY HISTORY- A PROSPECTIVE OBSERVATIONAL STUDY

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**ABSTRACT**
Asthma is a respiratory disorder prevalent in around 15% population of Pakistan. The global prevalence of asthma varies widely from country to country, however, ranges between 4.3%- 8.6%. The factors aggravating asthma in urban areas are well established. Still, there is limited data available from rural areas for the pattern of asthma, its aggravating factors and its association with family history. Therefore, this study was conducted to evaluate these factors. This descriptive and cross-sectional study was conducted in outdoor patient departments (OPD) of hospitals in Tando Adam, Sindh, Pakistan. In this study, 300 asthmatic patients were included. A non-probability convenient sampling method was adopted, and data was collected by filling a pre-designed structured proforma. The data showed that male patients were predominate with a rate of 56% as compared to 44% of females. Age and family history was not significantly associated with asthma. However factors environmental pollutants and smoking mainly associated with asthma. Quaderple therapy was most frequently prescribed method of treatment. Further studies with long term term follow-up will be required to confirm findings of this study.

**Key Words**: Asthma, aggrevating factors, Management pattern

## INTRODUCTION

Bronchial asthma is a long-term inflammatory state of the respiratory area related to bronchial hyper-reactivity and limitation of air-flow because of airway smooth muscle withdrawal frequently prompting trouble breathing and hypoxia (1,2,3). The pathogenesis of asthma includes eosinophil, mast cell activation and T-helper 2 (TH-2) lymphocytes invasion, IgE development by lymphocytes, and the advent of other inflammatory intermediaries, chemokines, and development factors via airway epithelium(4).

The causative and aggravating factors include a family history of atopy and environmental factors (5). The development of asthma is linked to natural triggers and endogenous biological factors (6). Thus, each individual with asthma has different pathological stimuli to start an episode of asthma (7). Commonly known triggers include strenuous work out and exposure to allergens such as dust, food, pet hairs, molds, quills, pollens, and chilly air. Modern synthetic substances (8) and tobacco smoke (9) may likewise have the potential to trigger asthma. Asthma affects approximately 334 million people worldwide, with 100 million expected to be affected by 2025(10, 11). The annually estimated overall mortality rate of asthma is reported to be 180,000 (12).

There is a remarkable variation in asthma prevalence in Pakistan. It ranges from 4.3% to 31.58% across different regions (11,13). According to a report from Pakistan, it was assessed that 5% of the total population was experiencing bronchial asthma. Asthma cases have grown over a decade and 2 million patients are now experiencing asthma, which incorporates a high level of youngsters, which is 20-30%, and the number is expanding by 5% yearly (14,15,16). Reported literature has shown association of age where in a study carried out in 1997 showed that 10% of the youngsters were experiencing asthma (17). Another investigation led in cowhide tannery plant in Karachi reported that 10.8% of the laborers were experiencing asthma (18). Though these studies were reported from urban areas or without any focus on rural areas, where is a less chance of interaction with environmental pollutions.

For management of asthma Two classes of anti-asthma medications are used anti-inflammatory and bronchodilators. Bronchodilators rearrange the bronchospasm of the prompt period of asthma while calming drugs restrains the inflammatory intermediaries of both chronic and immediate stages. The primary medications utilized as bronchodilators are β2-adrenoceptor agonists; additional drugs include Cysteinyl Leukotriene Receptor Antagonists, Xanthenes, and Muscarinic Receptor Antagonists. Failure to provide appropriate asthma treatment can lead to worsening symptoms and exacerbations (19), resulting in early and late consequences for the social, personal, and emotional well-being of asthma patients (20, 21). Therefore, 'asthma management' guidelines (22) recommend regular preventive management in order to reduce emergencies (21-26). However, it is reported that long term compliance of patients is not as per recommendations and at many places they are not provided with proper guidance as long they have to take medications.

Given the limited literature available showing asthma pattern in rural areas, association with environmental factors and family history, this study was designed evaluate these factors and in addition management pattern of asthma in hospitals of Tando Adam.

## METHODS

It was a descriptive observational study conducted in asthma patients reported in Tando Adam, Sindh, Pakistan. The study was conducted over a period of 12 months from 1st September 2017 to 31st August 2018. A total of 300 patients were included in this study . The patients suffering from asthma and visited the hospital during the study period were included in this study. The patients which were suffering from co-morbidities and also other diseases of respiratory tract were also excluded.A non-probability convenient sampling method was adopted . The demographic and pathophysiological data of patients was recorded by using a pre-designed structured proforma. The questionnaire type proforma having information regarding patient's history of the disease, gender, age, education, factors and management of asthma. The record of medicines was also obtained from the physician's prescriptions for management of the asthma.

## STATISTCAL METHODS

The data was analysed using Statistical Package for Social Sciences (SPSS version 21.0). All continuous variables are presented as mean and median with standard deviation, while categorical data was presented as frequency distribution. As this was a descriptive study no hypothesis was tested.

## RESULTS

A total of 1873 patients presented with respiratory symptoms and 300 (16%)patients were diagnosed with asthma by the treating physicians. . Out of these 168 patients were males (56%) while 142 (44%) were females.

**Age distribution of patients presenting with asthma**

The majority of patients in this study were between 49-58 years old (n=91 , 30.33%),  followed by the age groups  18-28 (n=72, 24%), 39-48 (n=66, 22%), 29-38 (n=41, 13.67%), and ≥ 58 (n=30, 10%) .

**Family history of asthma**

This study found that most patients with asthma have no family history (n=211,70.33%) while 89 (29.67%) patients reported to have a family history.

**Symptoms reported in asthma patients**

Cough was the most common symptom reported in patients with asthma in different combinations These combinations are presented in Figure 1.

**Factors aggravating asthma**

The most common factors in this study were smoking (n=56, 18.67%) , exposure to environmental toxins (n=53, 17.67%), exposure to chemicals (n=52,  17.34%) , dust exposure (n=39, 13%), air pollutants (n=36, 12%) , pets (n=18, 6%) , food allergy (n=18, 6%) , exposure to gases (n= 15, 5%) , and insect bite (n=13, 4.3%).

**Prescription pattern**

Out of 300 patients great majority (n=153) had quadruple therapy, and only 12 had monotherapy Figure 2 presents prescription pattern in the study population.



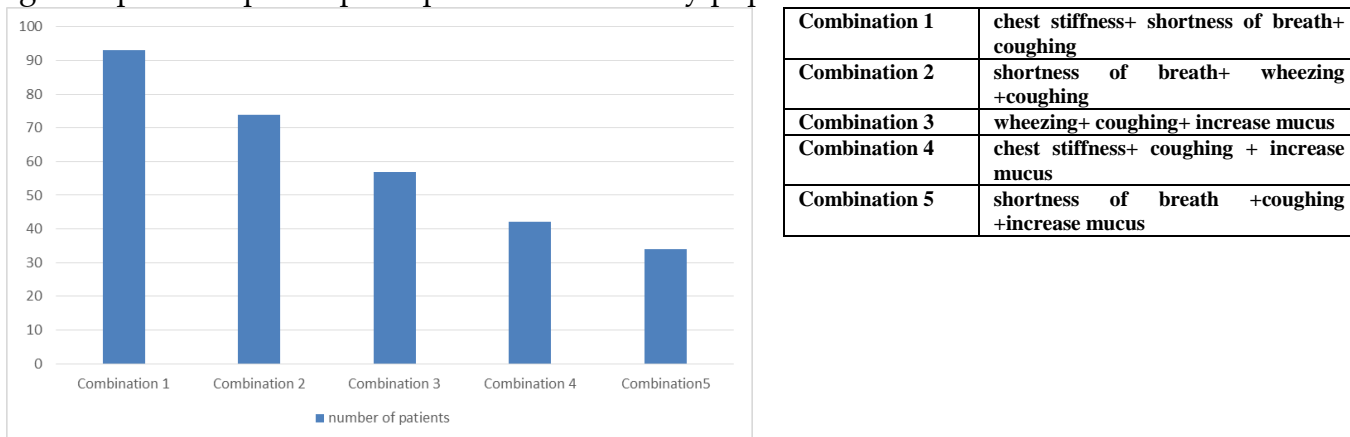| Combination 1 | chest stiffness+ shortness of breath+ coughing |
|---|---|
| Combination 2 | shortness of breath+ wheezing +coughing |
| Combination 3 | wheezing+ coughing+ increase mucus |
| Combination 4 | chest stiffness+ coughing + increase mucus |
| Combination 5 | shortness of breath +coughing +increase mucus |

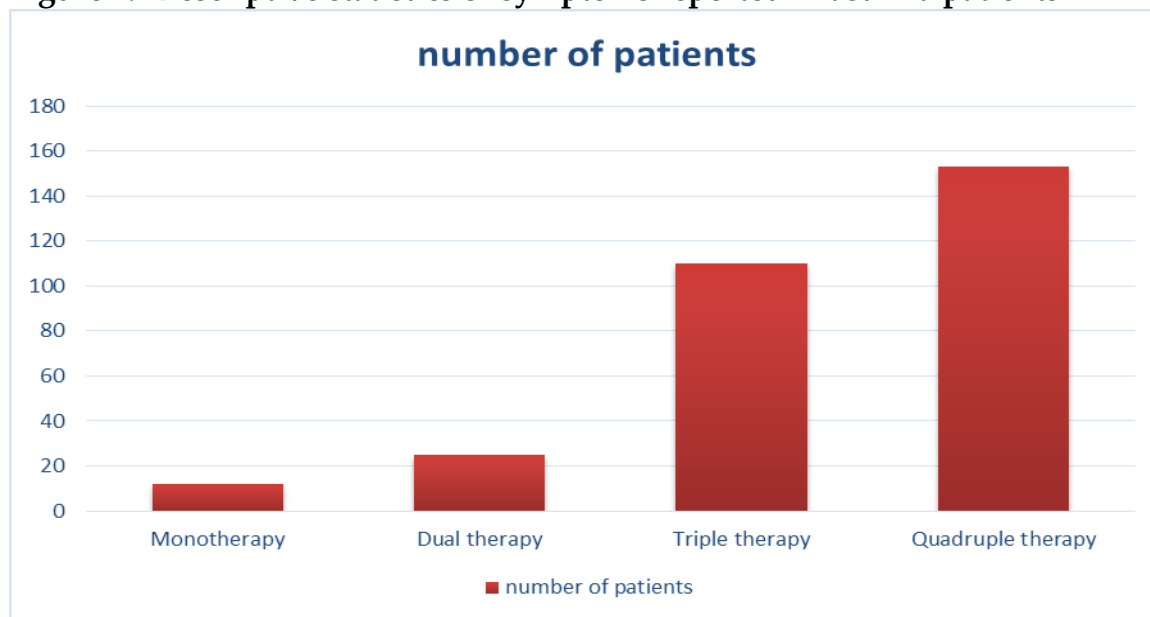**Figure 1.  Descriptive statistics of symptoms reported in asthma patients**



**Figure 2. Pattern of Prescription to the patients presenting with Asthma**

**Table 1. Factors aggravating Asthma in study population**

| S.No | Factors | No. of patient | Percentage |
|---|---|---|---|
| 1 | Dust | 39 | 13% |
| 2 | Smoking | 56 | 18.67% |
| 3 | Pollen grains | 36 | 12% |
| 4 | chemicals | 52 | 17.33% |
| 5 | Pets | 18 | 6% |
| 6 | Insect biting | 13 | 4.33% |
| 7 | Food allergy | 18 | 6% |
| 8 | Environment hazards | 53 | 17.67% |
| 9 | Gases | 15 | 5% |
| Total | | **300** | **100%** |

## DISCUSSION

Asthma is a common clinical condition affecting mainly respiratory system, however most of the studies from Pakistan are reported from urban areas. This research was conducted in both government and private hospitals in Tando Adam, Sindh, as rural city. This research has been performed in public sector and private hospitals of Tando Adam, Sindh. Total of 300 patients were included in the study to assess the prevalence and treatment trends of asthma in the said population. Those patients which were diagnosed and confirmed with asthma by physicians were included. It was observed from the study that asthma have 16% prevalence in Tando Adam. There is currently no cure, but management can help control the symptoms. The data was collected by filling structured proforma containing different questions. Most of patients observed in this study were suffering from symptoms which included shortness of breath, stiffness of chest and cough. There are 4 strategies to manage the asthma which are called as mono, duo, triple and Quadruple therapyaccording to symptoms patients have been suffered. Bronchodilator drugs followed by leukotriene antagonist and corticosteroids are prescribed in the therapy to overcome almost all of the symptoms. The main objective of the research was to regulate the prevalence and management for asthma in Tando Adam. It is remarkable how asthma affects the wellbeing delivery framework. Asthma is not only the most common incessant disease, but it's also the leading reason for emergency room visits, confirmations from the medical clinic, and non-appearance at school or work. Numerous studies have shown that asthma predominance has been investigated. Scandinavian countries having range from 1% to 1.5%, United States having 2-5% and in New Zealandup to 7%. (WHO 2017) (27). The prevalence of asthma is 16% in Tando Adam as per this research . From September 2013 to October 2013, the descriptive research was conducted in Lahore at Jinnah Hospital. According to that analysis of cases by age, a big figure of patientswere between 21 and 30 years n=35 (29%). Least n=14 (11.5%) were over 50 years of age with mean times of 33.5+-4.1. (Adil Hameed and colleagues 2014). However, most of the patients in this study were between 49-58 years old. 72 (24%) 68 were between 18-28 and 66 (22%) were between 39-48. 41 (13.37%) were between 29-38, 41 (13.67%) were between 39-48, and 31 (10%) were between 58-

onward. To assess the severity of asthma in Southern Punjab, Pakistan, the descriptive study was conducted in Pakistan. There were 81 cases of asthma among 120 patients (67.5%), and 39 patients (32.5%) were women. According to my study, males had more patients at 168 (56%) than females at 132 (44%). (Maryam. K, Muhammad T.J 2015) [28] A descriptive study was conducted in Maysore and gathered information it revealed that n=6268 patients were smokers and n=4289 were non-smokers. (Shivani R. et al 2013) [29]. According to my study, the most common factors are: smoking n=56 (18.67%); environmental hazards n=53 (17.6%), chemicals n=52 (17.33%), dust n=39 (13%), pets n=18 (6%), n=18 food allergy (6%), gases n=15 (5%) and insect bite n=13 (4.3%). A descriptive research study was done in Islamabad on asthma and hypersensitivities. It revealed that asthma is serious in Islamabad. (Muhammad A.W.et al 2009) (30). According to my research, more number of patients who participated in the study reported symptoms such as (shortness of breath +cough + chest stiffness), (n=93 31%) andthe patients reported symptoms like (cough +wheezing + shortness of breath)are (n=74 (24.67%), the patients reported symptoms such as (cough + increase mucous formation + wheezing) are (n=57 19%).

## CONCLUSION

The study has shown that asthma in our population was aggravated by environmental pollution and smoking. Thus strategies to prevent exposure of these factors is strongly recommended. Further studies to explore pathogenesis of these aggravating factors are recommended.

**Declaration:** This study is part of M.Phil Thesis of Nabila Channar conducted at University of Sindh.

**Ethical Consideration**: The study was approved by the local Research Ethics Committee

**Conflict of interest**

All the authors declared no conflict of interest.

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# SUCCEEDING GENERATION OF AUGMENTED REALITY TECHNOLOGY IN MEDICAL EDUCATION

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**ABSTRACT**

This review discussed augmented reality (AR), a new emerging technology seen everywhere in our daily lives. Augmented reality is widely used in healthcare, advertising, and engineering industries. It seems like the world will combine the real and the virtual worlds. From an educational perspective, augmented reality allows multimedia materials. This review aimed to provide reported trends and critical synthesis to identify gaps in existing literature and research areas. The PubMed, Web of Science, and Discover databases were used as sources for the review of the literature. This review included published studies reported in peer-reviewed research journals between 2019 to 2021. Augmented reality-based learning programs are widely used in medical schools around the globe because it provides distinct learning sources, such as remote learning and simulation-based learning. The benefits have increased in the recent COVID-19 pandemic, making it possible to give online. Education systems, including medical institutions, used augmented reality for the experiments and training of their students. This review also discussed how AR can improve the knowledge and skills of medical students.

## INTRODUCTION

Augmented reality (AR) is a subset of mixed reality that deals with real-world experiences to build digital methods or information. Barsom et al. 2016, mentioned that AR is an essential virtual reality. In practice, this is usually accomplished with tablet-based devices or headset devices (such as smartphones) in which the virtual objects are created surrounded by the real world. In addition to the auditory and haptic visual AR provides, it is also used for feedback which information is used in education to improve reality (1). The mixed reality allows and can switch the level of interaction experience to present the partial augmentation of the real world. The AR differs from virtual reality because its background is designed with computation. Still, AR and VR are at opposite ends of the assorted actuality spectrum. The field of AR emerged nearly two and a half decades ago (2). Thus it is a relatively new technology which is growly very fast and being used for educational purposes as well. It is also used in medical education and medical students' training so that they can understand easily. Students get a good experience and improve their learning content. AR can also be used to present complex medical concepts and data in an interactive way to make it understandable. For

example, AR can be used to create 3D models of organs or organ systems, allowing students to visualize and interact with them in a previously impossible way. Additionally, AR can be used to display medical images such as X-rays, CT scans, or MRI scans in a way that provides greater depth and detail than conventional 2D images. One of the significant advantages of AR technology in medical education is its ability to provide a safe learning environment without the risk of harming patients. Students can practice procedures and gain experience in a controlled environment before moving on to actual patient care. AR technology can also provide an immersive learning experience, allowing students to explore and interact with virtual anatomical models, surgical simulations, and medical equipment.

Furthermore, AR technology can facilitate remote learning and collaboration, allowing students to interact with instructors and peers in real time, regardless of their physical location. AR technology can also provide instant feedback, enabling students to assess their performance and improve their skills. Overall, the integration of AR technology in medical education holds tremendous potential to transform how students learn, practice, and acquire skills in healthcare. This review discusses essential practical aspects of the uses of AR in medical education in light of existing literature.

## A brief history of the use of augmented reality in medical education

Several programs have been successfully implemented using AR technology in medicine. These are broadly classified into two subgroups. The first involves treatment programs that assist patients and practitioners in a hospital or clinical setting, such as those used in therapeutics, rehabilitation, or surgical procedures. The second category contains exercise plans to improve educational institutes' training and awareness outcomes (3). This analysis focuses on these two aspected to evaluate the future usage of AR and highlight the need to develop and design other programs to improve learning and get suitable outcomes with this technology.

## Main functions of augmented reality

The AR is an emerging technology to generate real-world to virtual content; in other words, it is computer-generated content that improves the perception of the real world (4). Azuma et al. defined certain characteristics that are accepted to define AR systems (5-7).
1.      It mixes the existent world and simulated structure
2.      They are interactive in real-time.
3.      Enrolled in three dimensions.

The basic idea behind AR was to mix the view of the real world with the virtual layer to introduce the digital world. The virtual content can entice senses like touch, smell, hearing and sight (8, 9, 10).

The AR technology enhances the physical world features through a program application that utilizes one or more components (11). The program must be installed on the device before developing any AR image. There are two main types of AR computer execution: marker-based AR and markerless AR (12). Markerless AR employs 2D or 3D images, such as a sofa or a physical object like a building or people, which the AR computer program application can identify. Upon receiving input from the marker or object, the AR computer program application generate augmented virtual content and projects it onto the specified object (13-14). This immersive experience makes the additional information appear within the environment, creating an enhanced reality for the user(Figure 1).

## Materials and Methods for literature review:

This narrative review used PubMed, Google Researcher, and Scopus search engines. The keywords used for the literature search included "augmented reality", "therapeutic instructions", "understudy

experiences", and "learning outcomes". The articles published in English between January 2019 till December 2021 were selected.

## Related Work:

The AR-based medical programs have improved student experiences and learning outcomes. The AR-based training has the potential to viably and productively get restorative experts ready to practice in the real world (15). AR programs for learning in medicine are used to enhance learners' encounters, in expansion to giving a secure instructive environment and tending to particular proficient skills, as described in Figure 2.

Augmented reality has been found to provide a highly positive subjective experience for learning and can also be used for enjoyable and entertaining purposes. Games like Pokémon Go that utilize AR has become famous for the same reasons (16).
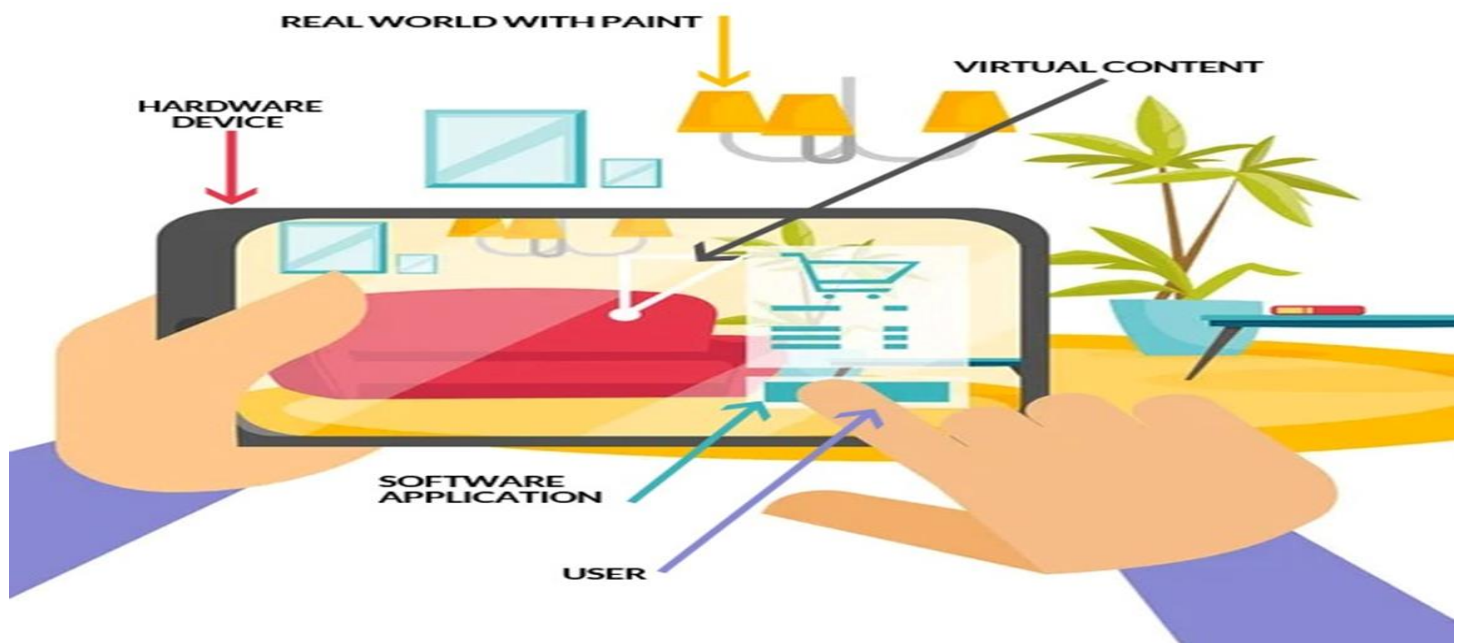


**Figure 1. Augment the physical world- A program application that employs one or more of different equipment components**
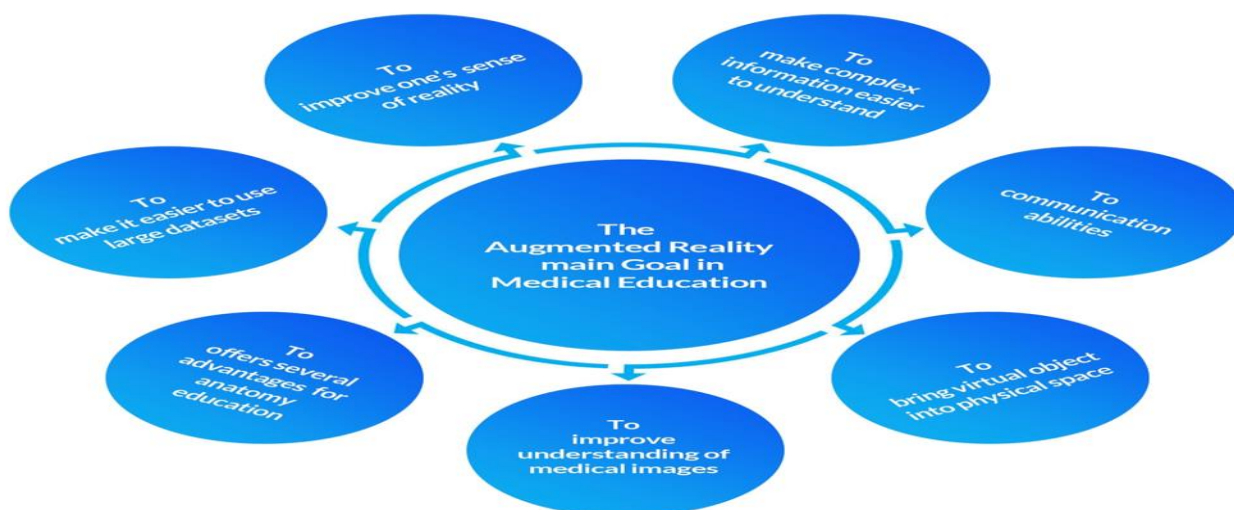


**Figure: 2. The primary objectives used in AR in medical education perspective**

Additionally, AR can potentially improve the delivery, presentation, and utilization of sensory systems in learning, three critical components of Mayer's cognitive theory of multimedia learning (17, 18). Students often report feeling more confident in their learning when using AR compared to conventional approaches, such as flashcards, due to their high level of digital literacy and familiarity with tablets and smartphones (19). Students of all levels are well versed in using devices for virtual reality for self-learning. The non-headset virtual reality programs show less negative effects, so VR still provides learning benefits. Moro and colleagues demonstrated that the structural anatomy runs on tablets using VR headsets achieved good learning outcomes in terms of anatomical test results. However, the AR tablet version showed fewer side effects such as dizziness, headache, discomfort and eye problems like blurred vision (20). The studies have confirmed that the AR-enhanced learning exercises were more likely to enhance student's theoretical knowledge and commonsense aptitudes resulting in improved examination results. AR-based learning prepares results in key zones, taking counting proficient information, cognitive and down-to-earth aptitudes, social abilities, advancement, competence, and inventiveness into account (21).

It is also reported that AR-based programs influence students' learning outcomes and experiences in association with the information and understanding, commonsense abilities, and social aptitudes domains of influence (Figure 3).



**Figure 3. AR-based programs affect students' learning outcomes and experiences in connection**

## Use AR to visualize human anatomy and Results

In depth understanding of anatomy is essential for medical students to understand physiological basis and pathological processes. Thus crucial for practising medicine (16). Dissection of cadavers was commonly used to teach anatomy in the past. To strengthen the learning of human body structure through visual and material encounters, anatomical disintegration is into sequential divisions of tissue layers and particular structures by evacuation of the territorial fat and connective tissue (17). Dismemberment lessons are helpful in a learning strategy since they offer a 3D picture of human structures. It advances information by providing a comprehensive set of anatomical structures and their relationships within an entire organism (18). However, this training method is rather expensive. Furthermore, no reliable large-scale data is currently available to support the efficiency of dissection classes in teaching anatomy (17). A massive quantity of knowledge on human anatomy and biological function is part of medical education (22). Although the creation of numerous digital systems, such as "virtual cadavers," has tremendously improved recently. AR has enabled medical students to improve their therapeutic understanding with advanced anatomical portrayal from all points, with a more comprehensive view typically differentiated from the real world accessed through a computer mouse and keyboard and operated on the computer screen (23).

## Challenges and future work

The utilization of AR platforms in medical education has advanced dramatically since they were initially used to treat orthopaedic problems. The cost of creating these interactive platforms is one of the most significant issues in the higher education sector (19). The high cost and the shortage of resources to satisfy the demands of the increasing student population hinder their use in medical education. Educators' largest challenge is ensuring that all children have equitable access to this digital technology. Along with the growing issue of social isolation linked to digital learning, the limited technology requirements for using AR in the classroom are another critique (21, 22). However, further developments in this area may benefit teaching students about subjects like human anatomy and physiology. For example, reading and visualizing information about nerve impulses and brain activity can help students retain information and better grasp human body physiology. It will be easier to combat the issue of separation that these AR stages may create for learners. These AR-interfaced books are a fascinating tool for students and instructors, providing a break from the static and gloomy text-only centred learning tool that standard reading material offers.

The emergence of AR has created exciting opportunities for medical educators to develop engaging and immersive educational programs that enable students to learn and experience the learning content. The COVID-19 pandemic has accelerated the adoption of digital teaching tools worldwide, emphasizing the importance of digital technologies such as AR in ensuring uninterrupted student learning. Using digital learning tools has the potential to revolutionize medical education and enhance the learning experience for students.

## CONCLUSION

The AR is widely used in various industries, including healthcare, engineering, entertainment and defence. Nowadays, the world combines the real and the virtual worlds. In educational perspective, the AR allows multimedia materials. Medical education has also shown a significant advancement by using AR where students learn basic sciences and clinical sciences more comprehensively. More robust studies directly comparing conventional and AR-based teaching methods will be required to make a firm conclusion.

**CONFLICT OF INTEREST:** Authors declare no conflict of Interest

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# BLOCKCHAIN IN HEALTHCARE: UNLOCKING THE POTENTIAL OF BLOCKCHAIN FOR SECURE AND EFFICIENT APPLICATIONS FOR MEDICAL DATA MANAGEMENT- A PRESENTATION OF BASIC CONCEPTS

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**ABSTRACT**

Medical data management presents significant challenges in terms of security, privacy, and efficiency. Blockchain technology has emerged as a promising solution to address these concerns in recent years. This comprehensive review explores the role of blockchain technology in secure and efficient medical data management. By providing a decentralized and immutable ledger, blockchain ensures data integrity, enhances privacy, and facilitates auditable access to medical information. The paper examines various applications of blockchain in medical data management, including electronic health records (EHRs), medical imaging, clinical trials, telemedicine, and drug supply chain management. It highlights the benefits and challenges of implementing blockchain in healthcare settings, discussing interoperability, consent management, scalability, and regulatory considerations. The review encompasses relevant research studies, industry initiatives, and real-world use cases to provide a comprehensive overview of the current state of blockchain technology in medical data management. The paper concludes with a discussion of future directions and potential areas for further research, emphasizing the transformative potential of blockchain in revolutionizing the way of medical data storage, sharing, and utilization.

## INTRODUCTION

Effective medical data management has been crucial throughout healthcare for delivering high-quality medical services, advancing research, and improving patient outcomes. Traditional approaches such as databases and distributed data management systems have played a significant role in storing, retrieving, and processing medical information. However, they have encountered security, privacy, data integrity, and interoperability challenges. Databases have been widely used in healthcare sector to store patient records, diagnostic results, and medical histories. These systems have provided structured storage and efficient querying capabilities, enabling healthcare providers to access patient information as needed. While databases and distributed data management systems have served healthcare reasonably well, they are not without limitations. Centralized databases can be vulnerable to single points of failure, exposing them to data breaches and unauthorized access. Furthermore, data silos created by disparate systems hinder seamless information exchange between healthcare providers, leading to fragmented care and a lack of continuity. To address the interoperability

challenges, Application Programming Interfaces (APIs) have played a crucial role in enabling data connectivity across various healthcare systems. Service Oriented Architectures (SOAs) based on Web-Services and Web-APIs facilitate data exchange between software applications and systems (1), allowing for interoperability and seamless communication. They provide a standardized interface for accessing and sharing medical data, fostering integration among electronic health records (EHRs), medical imaging systems, laboratory information systems, and other healthcare applications.

However, despite the role of APIs in promoting data interoperability, limitations exist. Healthcare APIs often face challenges with different data formats, varying data standards, and inconsistent implementation. Additionally, concerns regarding data privacy, security, and the lack of standardized APIs across different healthcare systems pose barriers to achieving full interoperability.

### Introduction to Blockchain

Blockchain technology has emerged as a promising solution to address challenges related to medical data management (2). Originally developed as the underlying technology for cryptocurrencies, blockchain offers a decentralized, transparent, and immutable ledger that can revolutionize the way medical data is handled. By leveraging cryptographic algorithms and consensus mechanisms, blockchain ensures data integrity, immutability, and resistance to tampering (3). Since blockchain is transforming various industries nowadays (4-7).

### Characteristics of Blockchain

Figure 1 presents blockchain's key characteristics: decentralization, immutability, security, transparency, trust and consensus, data privacy, scalability, smart contracts, interoperability and auditability. These characteristics collectively contribute to the unique value proposition of blockchain technology in a number of fields including healthcare.
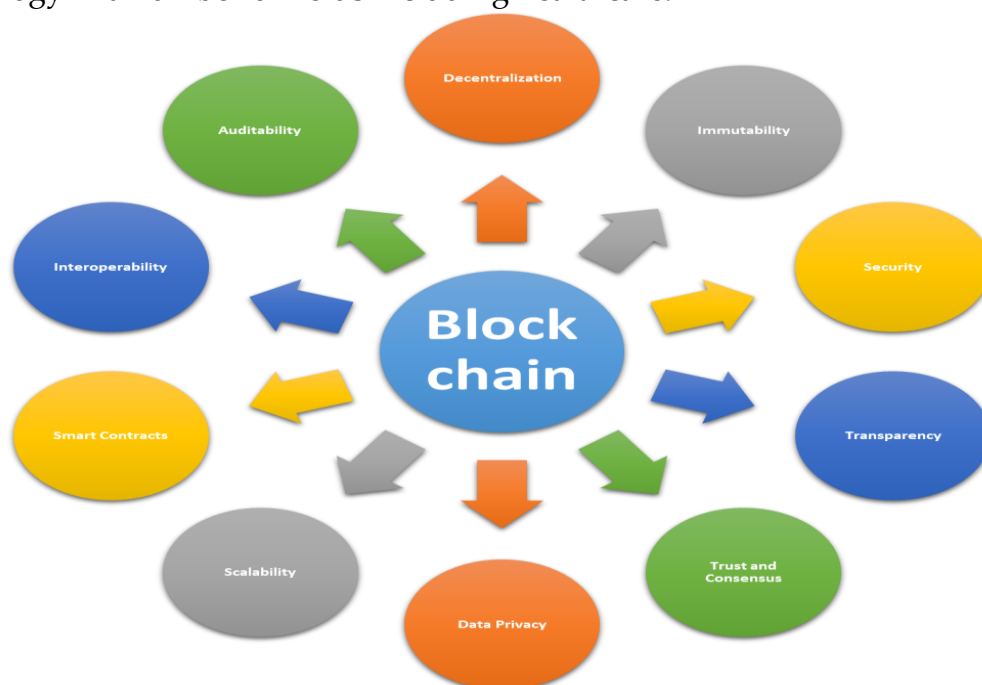


**Figure 1. Key characteristics of Blockchain network**

**Decentralization:** Blockchain works in a decentralized network, where there is no need to have a central control. This allows for peer-to-peer transactions and consensus among participants, promoting trust and transparency.

**Immutability:** As the data is added to the blockchain, it cannot be altered or deleted. The immutability feature ensures data integrity and enhances trust in the system.

**Security:** Blockchain operates upon cutting-edge cryptographic algorithms to provide highly secure data. Transactions are recorded in a transparent and tamper-resistant manner, making it difficult for unauthorized parties to manipulate or access sensitive information.

**Transparency:** Blockchain provides transparency by allowing all participants in the network to have access to the same information. Each transaction is recorded in a public ledger, promoting accountability thus reducing the risk of fraud.

**Trust and Consensus:** Blockchain relies on consensus mechanisms, like proof of work to authenticate transactions. This decentralized consensus ensures trust among participants without the need for a centralized authority.

**Data Privacy:** While blockchain promotes transparency, it also ensures privacy through the use of cryptographic techniques. Participants can maintain control over their personal data and determine the level of access granted to others.

**Scalability:** Scalability has been a challenge for blockchain technology due to limitations in transaction processing speed and storage capacity. However, various solutions are being developed to address these scalability concerns, such as off-chain transactions and layer-two solutions.

**Smart Contracts:** Blockchain platforms support self-executin agrrements having pre-defined conditions. Once the pre-defined conditions are meet, smart contracts automate processes and enable the execution of transactions.

**Interoperability:** Interoperability refers to the ability of different blockchain networks or systems to communicate and share data seamlessly. Standards and protocols are being developed to enhance interoperability and facilitate the exchange of information across various blockchain platforms.

**Auditability:** The transparent nature of blockchain allows for easy auditing of transactions. Every transaction on the blockchain can be traced and verified, providing an auditable record of events and enhancing accountability.

## Blockchain Data Structure

Blockchain works in a decentralized computer network (i.e. nodes), where each node maintains a copy of the entire ledger. A ledger is a collection of blocks, and each block consists of various transactions which contain data. In healthcare it will be patient's data, ensuring redundancy and resilience. The distributed nature of the network enhances security and eliminates the need for a central authority(8, 9).
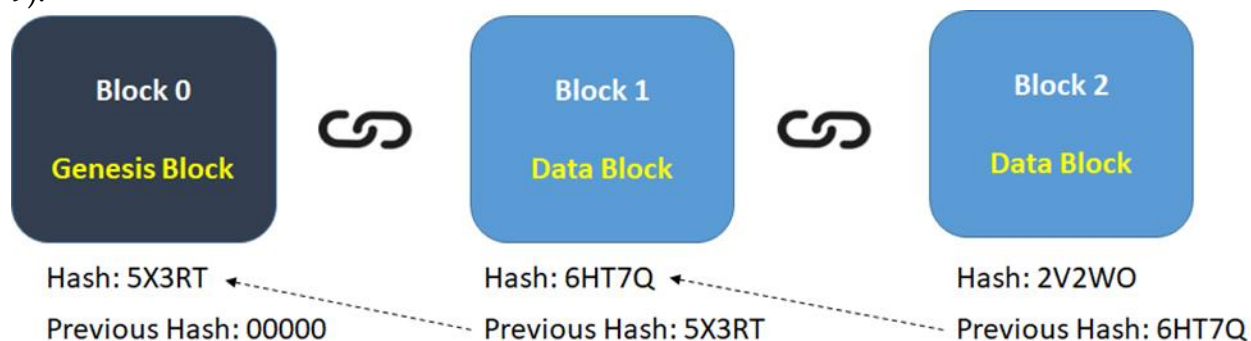


**Figure 2: Connected blocks forming a blockchain**

Each block contains different kind of data such as index, timestamp, hash, previous block hash and most importantly the data. Here, each block stores the information about its previous block's hash, which forms a chain of blocks. Some key components of blockchain are discussed here under. Figure 2 presents the format of block formation.

**Components of blockchain**

**Index:** The index or block number represents the position of the block within the blockchain. It is a unique identifier for each block and helps maintain the chronological order of the blocks in the chain.

**Hash:** The hash is a unique digital fingerprint generated by applying a cryptographic hash function to the data contained within the block. It serves as a digital signature that uniquely identifies the block and ensures its integrity. Even a minor change in the block's data would result in a different hash, alerting the network to potential tampering attempts.

**Previous Hash:** Each block (except the first block, also known as the genesis block) contains a reference to the hash of the previous block in the chain. This linking of blocks via their previous hash creates a sequential and tamper-resistant structure. Any modification to a previous block would require recalculating the hash of that block and all subsequent blocks, making it computationally infeasible to alter the blockchain undetected.

**Timestamp:** The timestamp represents the point in time when the block was created or added to the blockchain. It provides information about the order of events and helps maintain the chronological order of the blocks. Additionally, the timestamp adds a temporal dimension to the blockchain, enabling the tracking of events and ensuring that blocks are added in a logical sequence.

**Data:** The data component of a block contains the actual information or payload that is stored within the blockchain. In the context of a medical data system, this could include patient records, treatment information, diagnostic results, genomic data, or any other relevant healthcare-related data. The data is typically represented in a structured format and may be encrypted to protect patient privacy and ensure data security.

**Blocks:** Blocks are containers that store a set of data and transactions. Each block typically includes a unique identifier called a hash, a timestamp, and a reference to the previous block's hash. The blocks are linked together in a chronological order, forming a chain of blocks.

**Consensus Mechanism:** Consensus mechanisms enable nodes in the blockchain network to agree on the validity of transactions and the order in which they are added to the blockchain. Popular consensus mechanisms include proof of work (PoW)(10), proof of stake (PoS)(11), delegated proof of stake (DPoS), and practical Byzantine fault tolerance (PBFT)(12).

**Cryptography:** Blockchain relies on cryptographic techniques to secure data and provide privacy and authenticity. Public-key cryptography is commonly used for identity verification, digital signatures, and encryption of data within the blockchain. Cryptographic hashes ensure the integrity and immutability of the blocks(13).

**Governance:** Blockchain networks may have governance mechanisms in place to make decisions about protocol upgrades, changes, or other network parameters. Governance can be implemented through voting systems, committees, or community-driven processes to ensure the evolution and improvement of the blockchain network.

**User Interfaces and Wallets**: User interfaces and wallets provide an interface for users to interact with the blockchain network. They allow users to view their account balance, initiate transactions, interact with smart contracts, and manage their cryptographic keys (14).

These components collectively contribute to the functioning and security of a blockchain. The distributed network, blocks, consensus mechanism, cryptography, smart contracts, consensus incentives, governance (if applicable), and user interfaces form the foundation for building secure, transparent, and decentralized systems for various applications.

## Blockchain in Medical Data Systems

Blockchain technology can play a role in various areas of medical science. Here are some key areas where blockchain can be applied:

**Medical Data Management**: Blockchain can enhance the security, privacy, and integrity of medical data, including electronic health records (EHRs), medical imaging, patient-generated data, and clinical research data. It enables decentralized storage, secure sharing, and auditable access to sensitive medical information while maintaining patient confidentiality.

Interoperability and Health Information Exchange: Blockchain can facilitate seamless interoperability and standardized exchange of medical data among different healthcare providers, healthcare systems, and medical devices. It enables the creation of a unified and comprehensive patient health record by securely integrating data from disparate sources.

**Clinical Trials and Research:** Blockchain can streamline and enhance transparency in clinical trials by securely recording and verifying trial protocols, participant consent, and data collection processes. It can also enable secure sharing and collaboration among researchers, while protecting intellectual property rights and ensuring data integrity.

**Genomic Data Sharing:** Blockchain can provide a secure and decentralized platform for sharing genomic data among researchers, healthcare institutions, and individuals. It ensures data privacy by allowing individuals to control access to their genomic information while still facilitating collaboration and data-driven research.

**Immutable Storage and Traceability of Data:** Blockchain's immutability can ensure the integrity and traceability of genomic and proteomic data. By recording data transactions on the blockchain, it becomes difficult to alter or manipulate the data, thereby enhancing the reliability and trustworthiness of research findings and clinical outcomes.

**Personalized Medicine and Pharmacogenomics**: Blockchain can support personalized medicine by securely storing and managing genomic and proteomic data. Smart contracts on the blockchain can enable the execution of personalized treatment plans based on individual genetic profiles and proteomic markers, improving therapeutic outcomes and reducing adverse drug reactions.

**Drug Supply Chain Management:** Blockchain can improve the traceability and transparency of the pharmaceutical supply chain. It enables tracking the journey of drugs from manufacturers to patients, reducing the risk of counterfeit drugs, and ensuring the authenticity and quality of medications.

**Telemedicine and Remote Patient Monitoring:** Blockchain can facilitate secure and private telemedicine consultations, remote patient monitoring, and the exchange of patient data between healthcare providers and patients. It can enable patients to maintain control over their health data and grant temporary access to healthcare professionals.

**Medical Device Data Security:** Blockchain can enhance the security and integrity of medical device data by providing an immutable record of device configurations, usage logs, and maintenance history. It can help detect tampering attempts and ensure the accuracy and reliability of device-generated data.

**Healthcare Payment Systems:** Blockchain can improve the efficiency and transparency of healthcare payment systems, reducing administrative costs and minimizing fraud. It can enable secure and

automated transactions, streamlined claims processing, and accurate billing and reimbursement processes.

These are just a few examples, and the potential applications of blockchain in medical science are continually expanding. Blockchain's inherent properties make it an attractive technology for healthcare. Its decentralized nature eliminates the need for intermediaries and provides a secure and transparent environment for data transactions. By distributing data across a network of participants, blockchain can enhance data security, privacy, and interoperability. Moreover, the immutable nature of blockchain ensures the integrity of medical data, reducing the risk of data manipulation or tampering.

## CONCLUSION

This review presented basic concepts of blockchain data management system in healthcare, including EHRs, medical imaging, clinical trials, telemedicine, and drug supply chain management.

**CONFLICT OF INTEREST:** Authors declare no conflict of Interest

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# NON ISCHEMIC CARDIOMYOPATHY – A CASE REPORT

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**ABSTRACT**
Cardiomyopathies are a group of diseases characterized by the structural and functional abnormalities of the heart muscles in the absence of other illnesses that might be responsible for the observed myocardial anomaly. Hypertrophic and dilated cardiomyopathies are the most prevalent types. Rare types include restrictive cardiomyopathy and restrictive cardiomyopathy with arrhythmia. Dilated cardiomyopathy has a documented prevalence of 36 cases per 100,000 population in Europe and North America, and its yearly incidence varies between 5 and 7.9 cases per 100,000 population. Non-ischemic dilated cardiomyopathy, which causes heart failure, dramatically increases the global burden of cardiovascular diseases. For both men and women, acute dilated cardiomyopathy is mainly brought on by myocarditis. This case was present in Aga Khan University Hospital; and was selected to be reported. The diagnosis in the case scenario is non-ischemic cardiomyopathy associated with heart failure and pulmonary oedema.
**Key Words**: non-ischemic cardiomyopathy, Dilated Cardiomyopathy

## INTRODUCTION

Cardiomyopathies are a group of diseases characterized by the structural and functional abnormalities of the heart muscle in the absence of other illnesses causing the myocardial abnormality. Hypertrophic and dilated cardiomyopathies (DCM) are the most prevalent types. Rare kinds include restrictive, restrictive with arrhythmia. The pathogenesis of DCM includes ventricular enlargement and systolic dysfunction when neither severe coronary artery disease nor established aberrant loading conditions are present. It is regarded as one of the leading causes of heart failure globally. The DCM has a documented prevalence of 36 reported cases per 100,000 population in Europe and North America, and its yearly incidence varies between 5 and 7.9 cases per 100,000 population. The DCM appears to be more common in Africa and Latin America than in Eastern Asia, such as 14 reported cases per 100,000 in Japan, where it is more prevalent in comparison to Europe(1).

Previously reported studies have shown that non-ischemic cardiomyopathy is very common in young adults below the age of 50 years. Non-ischemic DCM, which causes heart failure, dramatically increases the global burden of cardiovascular diseases. For both men and women, acute DCM is mainly brought on by myocarditis. However, recent clinical and experimental data indicate that the pathophysiology and prognosis of DCM vary by gender (2). Here we present a relatively rare case of a young adult non-ischemic cardiomyopathy patient presenting with heart failure and pulmonary oedema.

## CASE SCENARIO

A 29 years old male patient was presented in the cardiology clinic with complaints of shortness of breath (SOB) and generalized oedema. The patient had SOB with fatigue and a productive cough for the last two months.

There were no known comorbidities; however, he had a positive family history of cardiac diseases. His father was diagnosed with Heart failure at the age of 20 years and died at 34 due to the complications. The patient's echocardiogram revealed a left ventricular ejection fraction of 10% with biventricular dysfunction. The patient was admitted electively for Left Heart catheterization, which later turned out to be normal. However, because of increased filling pressures and decreased cardiac output, an Intra-aortic balloon pump (IABP) was inserted and inotropic support was initiated. The patient was diagnosed with Non-ischemic Cardiomyopathy and transferred to CCU. Gradually, the patient developed anuric renal failure, prompting an increase in inotropic support despite IABP. Since the patient was a candidate for Heart Transplant, his family was recommended to look for a donor. Meanwhile, an atrial septostomy was advised for Left Ventricular unloading, for which the patient was transferred to the United States of America on family preference.

## Findings from Physical Examination and Clinical Presentation

On arrival, the patient's Glasgow Coma Scale was 15/15, oriented to time, place, and person. During physical assessment, the skin appeared cool and clammy. The cardiac evaluation revealed murmurs at the point of maximal impulse (PMI) consistent with an enlarged left ventricle. On respiration, bilateral equal air entry was accompanied by basal crept. Bilateral pleural effusion was evident by dull percussion at the bases. In the musculoskeletal System, tendon reflex was +2 with a range of motion limited at the right leg (due to IABP). Lymph nodes were non-palpable. The abdomen was soft and non-tender. No significant finding was noted in any other system. The patient was anuric during an assessment.

## Laboratory and diagnostic test findings with rationale

There are multiple diagnostic measures to rule out cardiomyopathy or associated risk factors depending on the symptoms. Initial evaluation of non-ischemic cardiomyopathy typically includes blood tests, radiological assessments such as Magnetic Resonance Imaging or Computerized Tomography scan, echocardiogram, electrocardiogram (EKG), Holter monitoring, and Cardiac catheterization. A summary of the investigations is presented in Tables 1 and 2.

**Table. 1. Summary of the cardiac of the patient**

| Diagnostic Measures | Results |
| --- | --- |
| Electrocardiogram | Heart rate > 90-110bpm<br>Atrial Fibrillation<br>Premature ventricular Contraction<br>Q waves |
| Echocardiogram | Left Ventricle Ejection Fraction 10%<br>Biventricular Dysfunction<br>Left Ventricular Thrombus |
| Cardiac Magnetic Resonance (CMR) | Dilated left ventricle<br>Trabeculation in stellate pattern<br>Thin myocardium apical anterior wall. |

## Differential diagnosis and current diagnosis with rationale

Cardiomyopathy is a broad term, and it leads to many cardiac complications. As it can either be ischemic or non-ischemic, sometimes it gets difficult to distinguish between both disorders. Furthermore, cardiomyopathy is divided into four types; dilated, hypertrophic, arrhythmogenic, and restrictive cardiomyopathy (3). The final diagnosis in the case scenario is non-ischemic cardiomyopathy associated with heart failure and pulmonary oedema. Non-ischemic dilated cardiomyopathy, which accounts for >50% of all heart transplant surgeries, is currently the leading cause of progressive heart failure(4).

## Management of the Non-ischemic Cardiomyopathy

The causes of non-ischemic dilated cardiomyopathy determine the course of treatment. Treatment aims to lessen signs and symptoms, enhance blood circulation, and avoid additional damage to the heart. Apart from medical management, surgical implants are also used as part of a dilated cardiomyopathy treatment plan to improve cardiac contractility, ultimately increasing the cardiac output and minimizing the manifestations(5).

**Table 2. Summary of Hematological Investigations of the Patient**

| HB | 10.6 | K | *4.9 |
|---|---|---|---|
| HCT | *32.8 | Na | 138 |
| RBC | 6.52 | HCO3 | 24.8 |
| WBC | 21.5 | Cl | 101 |
| Platelets | *140 | Ca | 9.1 |
| PT | 12.7 | BUN | *27 |
| APTT | 23.5 | Cr | *2.8 |
| INR | 1.0 | Trop-I | *204 |

## Pharmacological Therapy

A number of drugs are available, and a combination is preferably used to treat dilated cardiomyopathy and avoid any further complications. Table 3 shows the typical medications used in the treatment plan for non-ischemic cardiomyopathy (5).

**Table 3. List of drugs available for treatment of cardiomyopathy**

| Drug Class | Mechanism of Action |
|---|---|
| Angiotensin-converting enzyme (ACE) inhibitors (lisinopril, enalapril, etc) | Reduces afterload through peripheral vasodilation. |
| Beta Blockers (atenolol, metoprolol, carvedilol, etc) | Reduces cardiac workload and oxygen demand that occurs as a response to sympathetic activation. |
| Angiotensin receptor blockers (ARBs) (losartan, candesartan, etc) | Inhibits Vasoconstriction and Myocardial fibrosis |
| Hydralazine/nitrate combination | Acts as a vasodilator |
| Diuretics | Eliminates excess fluid from the body (Volume overload) |
| Selective Antagonist Eplerenone | Attaches selectively to the mineralocorticoid receptor, limiting the binding of aldosterone and preventing sodium reabsorption as well as other harmful aldosterone related processes. |
| Ipratropium Bromide | Anticholinergic Bronchodilator |

## Non-Pharmacological Treatment

Non-pharmacologic treatments for non-ischemic cardiomyopathy include both device therapy and surgical intervention. Implants that are frequently utilized to treat non-ischemic cardiomyopathy involve the following options:

- *Implantable Cardioversion Defibrillator:* Used as a secondary prevention in patients with ventricular arrhythmias regardless of the involvement of coronary syndrome.
- *Cardiac Resynchronization Therapy:* Monitors cardiac activity such as mitral regurgitation, cardiac index, and Left Ventricular volume. It is recommended to improve quality of life.

Apart from Device therapy, some surgical procedures are performed to temporarily improve cardiac activity and reduce further complications, such as Mitral Valve Annuloplasty, Left Ventricular Assist Device, and Atrial Septoplasty. Since there are not enough studies to support the long-term benefits of these procedures, Cardiac transplantation is ultimately the ''gold standard'' for the treatment of end-stage cardiac failure(5).

## DISCUSSION

After reviewing the case, genetic factors emerged as the root cause of non-ischemic cardiomyopathy for this patient. The pathogenesis of heart failure in DCM includes immune-mediated processes, peripartum cardiomyopathy (PPCM), endocrine and metabolic disorders, hereditary reasons, direct cardiac injury from viral or toxic agents, and genetic factors. A genetic factor can be found in 30–50% of cardiomyopathies cases and up to 40% of DCM patients. However, this fraction is likely overestimated, given the variability in disease penetrance and clinical presentation (1).

Given its higher spatial resolution, cardiac magnetic resonance (CMR) is the gold standard for determining ventricular ejection fraction and volume. CMR may accurately diagnose a number of diseases, including cardiomyopathies. In contrast to an echocardiogram, CMR has the potential to preclude other possible causes of the cardiomyopathies like amyloidosis, coronary artery diseases and iron overload. Reduced cardiac function, ventricular enlargement, and thinning of the myocardial wall can be easily seen on CMR. Due to its capability to enable the evaluation of numerous different tissue features in a single test, cardiac MRI is essential to evaluating patients with cardiomyopathy(6).

### Critical points for reflection

After going through this patient's history, we selected this patient for our case study because we felt that non-ischemic cardiomyopathy in young adults is reported more frequently. After going through the patient history and literature, we found that genetics and heredity can be the leading cause of non-ischemic cardiomyopathy, and its early detection can increase the chances of survival and prevent complications. For this combination of situations there is limited literature available. Thus further studies to assess risk factors, early detection methods, and screening protocols needs to be studied.

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