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## Mukherjee's Equation: An Equation to Calculate GFR of an Obese Asian

# QR CODE

### DATTATREYA MUKHERJEE

### Dear Editor,

Glomerular Filtration Rate [GFR] is an essential value to understand the condition of two kidneys.<sup>1</sup> Currently we are using different formulas to calculate it. One of the formulae is 1973s Cockcroft-Gault formula.<sup>2</sup> The formula is:

### C<sub>Cr</sub>={[140-age] x wt}/S.Cr x 72

Wherein

- CCr (creatinine clearance) =mL/minute, this reflects the GFR
- Age = years
- Weight = kg
- SCr (serum creatinine) = mg/dL

Currently the most used formula is 2009 CKD-EPI creatinine equation<sup>3</sup> which has parameters like SCr, Age, Gender, Race.

Now, I have studied and realized that we are missing with an important factor, that is height which is a very important demographic factor. Several studies have shown that BMI is inversely proportional to GFR.<sup>4</sup> So, after calculating I am proposing an equation which has height as a measuring factor. This equation will be called Mukherjee's equation. The equation is:

GFR =[2100-age]/[0.72 x S.cr x BMI]

Wherein:

- BMI=Weight in Kg/Hight in m<sup>2</sup>
- Age in years
- S.Cr in mg/dl

### Points to be noted:

This formula is for Asian patients
 Age is more than 18 years

- 3. Only for obese patients, BMI>30
- 4. For female, the value will be multiplied by 0.8

I am proposing this equation and, in my calculation, I have found some differences with the conventional one. I believe this equation will give more precise result than the conventional one. Through this equation, I have tried to create a bridge between Cockcroft and 2009 CKD-EPI. Although, a clinical trial is needed to validate this equation. Through this article, I am first proposing my equation, Mukherjee's Equation in front of the scientific world.

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**OR CODE** 

### Paying Obeisance to the Humble "Coconut": A Short Commentary

SHAILESH JAIN ២

Every year, on 2<sup>nd</sup> September, the world unites to thank the humble "coconut" for its immense benefits by observing the "World Coconut Day". The ever-popular coconut, apart from its other uses, has proven to have various health benefits.

Scientifically known as Cocos nucifera L., the coconut is a tree cultivated for its nutritional and medicinal values. Other products of coconut include tender coconut water, copra, coconut oil, raw kernel, coconut cake, coconut toddy, coconut shell and wood based products, coconut leaves, coir pith etc and these products are found in day to day use.<sup>1</sup> Due to its many uses, it is often referred to as the "tree of life".<sup>2</sup>

The coconut fruit generally consists of 51.7% kernel, 9.8% water, and 38.5% shell and is an integral part of many South Asian diets.<sup>3</sup> Beyond its usage in cooking, coconut oil has attracted attention due to its hypocholesterolemic, anticancer, antihepatosteatotic, antidiabetic, antioxidant, anti-inflammatory, antimicrobial and skin moisturizing properties.

An important component of the coconut, coconut water, in its natural form is a refreshing and nutritious beverage consumed widely due to its beneficial properties to health, mostly which are based on various cultural and/or traditional beliefs.<sup>4</sup> Since ages, coconut water has been used for oral rehydration and even so for intravenous hydration of patients in remote/rural areas.<sup>5</sup> Coconut water may also offer protection against myocardial infarction.<sup>5</sup> As per the results of Alleyne T et al. (2005), regular consumption of either coconut water or mauby (a liquid extracted from the bark of the mauby tree, Colubrina arborescens), or particularly, a mixture of them, is effective in bringing about the control of hypertension.<sup>6</sup> It also has been reported that Tender Coconut Water (TCW) and mature coconut water can reduce the occurrence of lifestyle diseases by reducing the risk of heart disease and has significant hypocholesterolemic, antioxidant and antithrombotic effects. Other researchers also have documented that immature coconut inflorescence helps lower blood glucose in diabetic rats.<sup>7</sup>

**Medicinal Values:** The various medicinal effects of coconut are as follows:<sup>1</sup>

- Electrolytic effect
- Antidote effect
- Antioxidant effect
- Cardioprotective effect
- Antithrombotic effect
- Antiatherosclerotic effect
- Hypolipidemic effect
- Anticholecystitic effect
- Antibacterial effect
- Anticaries effect
- Antidermatophytic effect
- Antiviral effect
- Antifungal effect
- Antiprotozoal effect
- Anticancer effect
- Immunostimulatory effect
- Antidiabetic effect
- Hepatoprotective effect
- Disinfectant effect
- Insect repellent
- Eco-friendly biodiesel
- Hormone like effect

The coconut palm has a significant effect on the rural



© Shailesh Jain. This is an open access article distributed under the terms of the Creative Commons Attribution License CC-BY-NC 4.0, which permits unrestricted use, distribution and reproduction in any medium, provided the use is not commercial and the original author(s) and source are cited. Submitted on: 22-Sep-2021; Accepted on: 19-Oct-2021 economy of many coastal states where it is grown extensively and provides income to more than 10 million people. Therefore, it is of little amusement that the coconut culture is spreading even to nontraditional belts that, until recently, were considered unsuitable for the purpose.

### **CONCLUSION**

This short commentary is a tribute to the humble coconut and educate people regarding the immense benefits of this humble "fruit". It is therefore only justified that a day is dedicated on the global level to celebrate the benefits provided by coconut and its products. Through further clinical and evidence-based studies, it is only a matter of time that coconut finds its way into the regular medical practice and drugs are prepared using its extract.

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### **Evidence Based Decision Making: A Review**

### TWESHA HUIDROM\*1, RAVNEET MALHI2 🖻

A B S T R A C

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In today's era, many of the decisions are based upon gut feeling, intuition, or instinct rather than relied on actual scientific data and facts. It's important and essential to do the needful based on facts and not feelings for the best possible outcomes. Evidence based decision making in the field of healthcare describes the integration of basic rules of evidence as they evolve into implementation in daily practices. In dentistry, the principles of evidence-based decision making as well as a very common clinical dilemma to make a decision on whether to save and preserve the natural tooth or to extract and replace it with an implant or any sort of prosthesis is often experienced by a clinician easily. The need of evidence plays a very important role in making decisions. It helps provide a better outcome which will result in fewer casualties.

KEYWORDS: Evidence-Based, Medicine, Dentistry, Decision, Error

### **INTRODUCTION**

"Human history is mostly the story of error and accident."

-Michael A. Ledeen

In today's advanced era, many of the decisions are based upon gut feeling, intuition, or instinct rather than relied on actual scientific data and facts. Though presence of facts and figures is already available but due to the lack of an individual's interest and resistance towards information it results in errors and problems. Everyone, be it a person, a society or an establishment has made errors in the form of imprecise beliefs or decisions. In earlier times, errors and mistakes in evidence-based decision making must have been greater than that in the recent times. Before, the research and the findings were far lesser than that which we can find today.<sup>1</sup> Written material is widely accepted and is like the Holy Grail for evidence-based decision making. It gets updated and new research findings are added so that errors can be decreased giving us better results. Errors can occur anywhere in the process of decision making. It can be on an individual level by considering beliefs and interpretation of information on their own and can result in inaccurate application of the process. Disposition and aversion to information can also result in errors while making decisions. Our main aim is to identify and reduce these errors so that the quality and quantity of the result is not hampered.

The categories which can be included for improvement are basically reduction in time, cost, effort, dispute, disease and many other possibilities.<sup>2</sup> We know that eliminating all the errors in one go is not possible. But the severity and the frequency can be reduced and should be considered our main goal. Some of the prerequisites which should be followed at an individual level include accepting the fact that there may be errors in any evidence; the individual should be willing to identify the errors and lastly they have to accept that research attempts to obtain justifiable facts and evidence.<sup>3</sup>

Thus, it's important and essential to do the needful based on facts and not feelings for the best possible outcomes. Evidence-based decision making (EBDM) is an ideal model which we can use to ensure that you are considering relevant facts and not something that is not proven. Evidence based decision making is a process that helps in making decisions about a program, practice, or policy that is grounded in the best available research evidence and informed by experiential evidence from the field and relevant contextual evidence. All the information present in scientific research with good outcome should always considered while taking a decision. Three categories which are mainly the part of this framework are contextual evidence, best available research evidence and experiential evidence.4

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The decision-making process has three main stages. First is the collection of evidence which basically means gathering evidence from the best available research. Second is the interpretation of the evidence. Third and the final stage are applying the things that we have learned from the evidence. In this we are considering all three stages while making the decision based on the evidence to prevent any issue or problem before it occurs. The characteristics of the decision-making process includes transparency, participation, openness, skilled leadership, facilitation and a definite process. We need to get the best outcomes using these characteristics. We need to know for a fact that every scenario is unique and the evidence differs from situation to situation.<sup>5</sup>

Evidence Based Decision Making in Medical Field: Historically, evidence based medicine goes back to the 1700s, though it was not clearly explained and advanced until the early 1980s. Evidence based medicine was initially known as 'critical appraisal' to describe the integration of basic rules of evidence as they evolve into implementation in daily practices. Evidence based medicine is defined as a conscientious, explicit and judicious use of current best evidence in making decisions about the care of individual patients.<sup>6</sup> They are defined based on 4 important and basic categories, which involve acknowledgment of the patient's problem and making of a structured and well layered clinical question, thorough research in medical literature to bring out the best available evidence to answer the question, critical appraisal of all available evidence and usage of the evidence with all facets and contexts of the clinical conditions. Recent evidence-based decision making research has indicated that the framework and functioning of healthcare facilities has contributed to an organization's functional success by improving and increasing safety, standard and their regulation process. There is very little information accessible about the financial returns of evidence-based investments; such investments are eliminated during the decision-making process.<sup>6,7</sup>

Healthcare facilities are very costly, dangerous, inefficient and not easily accessible in many places. Though the government has provided many provisions for the betterment of healthcare in places where easy access of healthcare is hard but awareness in a majority of population is still lacking. Many issues arise from a good amount of people ignoring all the pleas from the designated healthcare workers.<sup>5</sup> The

evidence that has to be collected from the population is decreased due to this issue. Without surveying and collecting evidence, research in that field is going to be a very difficult process. Surveys and research are a very important source of information and updates which are accessed and used by the healthcare professionals to help them in decision making. Updating of such research and content plays a very major role in decision making. In a field where past research with proof and evidence tends to the need to have good results and also good prognosis of the individual, evidence-based decision making is really necessary. Majority of the healthcare professionals are survived by such written material. If the content is written and widely accepted with proof of it being mostly successful, then it is easily considered in the process of implementing the evidence into the treatment or decision making. In a health care setting, be it a private clinic or a hospital, the complicated cases which have a multifaceted treatment process, require an extensive list of evidences and maybe more professionals from a different medical field to create a treatment plan which will give the best prognosis and even help save a life.4,6,7

Sometimes it is possible that going by the book and following the protocols may turn out to be a risk for the patient and he or she may even lose his or her life. So, we do know for a fact that evidence in a lot of cases may not turn out to be useful or helpful for the patient. It can be the worst decision of his or her life and also the medical practitioner who is the one taking the decision will be at a tight spot from that point onwards. There are a lot of things that the medical practitioner has to explain and comply with after taking a decision based on the facts and figures, which in turn didn't help in preserving one's life. Evidence based decision making also helps in medico-legal issues.<sup>8</sup> In very rare cases the gut feeling of a medical healthcare professional works wonders with the help of evidence. Like if the doctor has all the necessary reports and he knows his way to go about for the treatment but still chooses a different way based on his feeling and intuition, it can turn out be a really bad decision for the patient's life. There's a 50-50 chance when feelings and intuition are followed. But there is 80-90% of a chance that the treatment goes well if we go by the evidence and follows all the protocols. Medical field is literally so vast and big. The need of evidences, research and updating of the research is a sole necessity to make decisions in the

medical field.4,6,8,9

**Evidence Based Decision Making in Dentistry:** Usually in dentistry the complicated cases of endodontology, periodontology and oral rehabilitation often pose a dilemma in the clinician's mind as to how they can tackle the situation to give the correct treatment plan. The principles of evidence-based decision making as well as a very common clinical dilemma to make a decision on whether to save and preserve the natural tooth or to extract and replace it with an implant or any sort of prosthesis such as a fixed partial denture is often experienced by a clinician easily. Evidence through investigations and research can prove to provide better closure for the treatment plan.9 This will ultimately help in the better diagnosis of the treatment that has to be rendered to the patient. Many cases require a multifaceted treatment approach for the prognosis to be good with least number of complications. The outcome of the treatment may not be compromised if the main goals of the treatment are achieved. However, in a lot of cases where complications hamper the main treatment goals, decrease in predictable outcome is seen or anticipated. The rule of the thumb or the main principle in dentistry is to put a good amount of effort in preserving the natural teeth. Any different treatment outcome may lead to confusion when we try and compare two different treatment alternatives.

Therefore, it should be fully based on the correct measurements of the different treatments. Other factors like patient's preference, prosthetic/periodontal/endodontic considerations or long-term prognosis should be considered and should be recognized in the clinician or practitioner's final decision making.<sup>10,11</sup>

In a dental practice setting the use of clinical practice guidelines and protocols organized by the decision trees is the most ethical and successful way to go about in that setting? Now what is a decision tree is the question? A decision tree assists the dentist when he or she is presenting with the conditions and patient values are less possible in recommending treatment manners whose benefits and harms are varying and unknown. Best proof based on the 'average patient' is incorporated in the decision tree. Chances, utility and economic data are calculated and surveyed in providing the patient with informed and personalized choices of care. Evidence-based decision-making accounts in a process in which an individual patient is enlightened of the best probable evidence and all pertinent options. The result of the process is that patient serviceability and cost apprehensions are fully addressed in enhancing the clinical decision. In dentistry, evidence-based decision making is a discipline that provides optimum, clear-cut evidence to dentists and their patients in shared decision making.<sup>9,12</sup>

In the recent scenario, dentists are being provided with the training of being able to adopt the role of translational researchers in developing evidence based dental practices. Realistically, evidence-based dentistry is not feasible in its current form for the purveying of labor intensive provisions that distinguish recent dental practice. Evidence based decision making also conceptualizes a team proposition in explaining issues and solutions to change the recent dental practice. All these changes integrate a practice that involves an electronic tabulation, centralized and generalized database, knowledge management software and manpower in optimizing effective and useful oral healthcare to dental patients. Scientific, pertinent evidence is important in clinical care, policy making, controversy resolution and law. As a result, evidence-based practice brings together relevant, trustworthy information by in order collecting, inspecting and transferring research findings into clinical, management and strategy areas. One of the main important things in evidence-based decision making is to assess the available evidence to judge what is bad and what is good or better. The available evidence should be graded by the strength of the proof and evidence. The levels of evidence are often considered when applying it. The hierarchy is usually followed because older information keeps getting updated and the newest evidence is often the best evidence. In these levels of evidence randomized trial controls are mostly considered as high level of evidence. In 'Oxford centre of evidence-based medicine' the hierarchical system of classifying scientific evidence is elaborated very well. It provides an evident comprehension regarding the scientific evidence. This may lead to surprising conclusions that may dispute common concepts and even show a reverse pyramid of scientific evidence.10,12,13

Conclusion: The need of evidence plays a very important role in making decisions. It helps provide a better outcome which will result in fewer casualties. We know that newer technologies and recent advancements in scientific researches' will add to the legitimacy of the evidence which will ultimately result in making better decisions. Better decisions may not always lead to an accurate outcome but in most cases it does help in achieving the goal which is required. We should work on reinforcing and confirming the already present research and findings so that referring the research by the book will result in very fewer casualties.

"The delivery of medical care is to do as nothing as possible"

House of God-1979

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### The Wonderful DMARD with Multiple Toxicities

### YASHIKA KAUSHAL<sup>\*1</sup>, RATIBHA KAUSHAL<sup>2</sup>, ISHA SHARMA<sup>3</sup>

Methotrexate is a type of disease-modifying anti-rheumatic drug (DMARD). It is used to reduce activity of the immune system for people who have certain conditions. Methotrexate is a chemotherapy agent and immune system suppressant. Its use may be limited by concerns regarding its adverse reactions. The occurrence of adverse drug reactions in some cases leads to the therapy discontinuation. Although adverse drug reactions (ADR) of methotrexate generally do not pose a serious threat to the health of patients and a reduction in the dose of methotrexate leads to their elimination, in some cases severe toxicities of the drug occur unpredictably. These facts explain the need for close monitoring of the patient's condition and the identification of potential risk factors for drug toxicity on the part of different organs and functional systems. The purpose of this review is to detail about safety and tolerability of methotrexate.

KEYWORDS: Methotrexate, Adverse Drug Reactions, Toxicity, Patient Safety

### INTRODUCTION

Methotrexate is one of the drugs of choice for systemic treatment of moderate to severe forms of multiple disorders. Methotrexate is a highly effective drug that has been used successfully for more than 50 years to treat skin diseases.<sup>1</sup> At present, methotrexate is also used for the treatment of other dermatological diseases, such as vasculitis, bullous dermatosis, and lymphoproliferative diseases.<sup>2</sup> Methotrexate has proven to be a highly effective drug, but half of patients experience ADR during treatment. The pathogenesis of most ADR of methotrexate is based on its cytotoxic effect on rapidly dividing body cells, primarily the cells of the gastrointestinal bone marrow, tract, and hepatocytes. Methotrexate toxicity effects all the major organs of the body.

Gastrointestinal disorders are the most common ADR of methotrexate: 18.2% of patients report nausea and vomiting; 11.1% have ulcers of the oral mucosa and other mucositis; 7.5% have abdominal pain; and 6.6% of patients note intestinal functional disturbances.<sup>3</sup> The primary mechanism of ADR with methotrexate therapy is inhibition of folate metabolism in tissues with high cell proliferation, with a high need for purines, thymidine, and methionine. Since gastrointestinal epithelium is characterized by a rapid rate of cell population turnover, folate deficiency is the major mechanism in the development of this ADR group.<sup>4</sup> The incidence of gastrointestinal ADR may be influenced by the patient's genetic characteristics, namely the presence of polymorphisms in the genes encoding the methotrexate transporter proteins.

Hepatotoxicity of methotrexate is one of the most significant ADR of the drug.<sup>5</sup> The hepatotoxic effect of methotrexate is mainly manifested by two ADR groups: elevated liver enzymes and development of structural changes in the liver.<sup>6</sup> Liver enzyme elevations occur in 10% of all patients taking methotrexate on the average.

Liver fibrosis usually develops with a long-term use of methotrexate: such structural changes in the liver occur in 25% of patients taking methotrexate for more than 5 years.7 While testing liver biopsy specimens from patients with rheumatoid arthritis treated with methotrexate, accumulation of polyglutamate forms of methotrexate and folate deficiency was found in cells, which may indicate that the hepatotoxicity of methotrexate is associated with folate depletion due to the action of polyglutamate forms of the drug.<sup>8</sup> Polyamine synthesis, accumulation of adenosine and deoxyadenosine, impaired metabolism of homocysteine and purines are also thought to play a role in the formation of the hepatotoxic effect of

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methotrexate. According to the results of studies in mouse models, the cause of methotrexate-induced liver fibrosis is the stimulation of collagen synthesis by the accumulation of adenosine: adenosine binds adenosine A<sub>2</sub> receptors on the hepatic fat-storing stellate cells, which are potentially fibrogenic and stimulate collagen production.<sup>9</sup> Methotrexate triggers the lipid peroxidation process, which leads to the synthesis of reactive oxygen species and damage to liver cells. Possible risk factors for these ADR should be considered when predicting the risk of methotrexate-induced hepatotoxicity.

Other risk factors for increased hepatotoxicity of methotrexate include persistent elevated aminotransferases, alcohol use, chronic liver disease, history of hepatotoxic drug use or exposure to hepatotoxic substances, hereditary predisposition to genetically determined liver diseases, alpha-1 antitrypsin deficiency, and hemochromatosis.<sup>6</sup> To predict the hepatotoxicity of methotrexate, a complete blood count, liver enzyme testing, serologic studies to identify hepatitis B and C biomarkers, and ruling out other risk factors for increased hepatotoxicity, including genetic ones, are required before starting therapy. Since the drug is excreted by kidneys and impairment of their function may increase the risk of hepatotoxicity, creatinine and urea levels should be assessed. Regular monitoring of aminotransferases as an early and reliable marker of liver injury is now considered sufficient in the first stages of therapy. Additional specific tests to assess liver status are recommended in case of risk factors for hepatotoxicity or abnormal liver chemistry.

Some patients develop hematologic abnormalities, such as myelosuppression manifested by macrocytic anemia, leukopenia, lymphopenia, thrombocytopenia, hypogammaglobulinemia, and pancytopenia. The mechanism of methotrexate-induced thrombocytopenia is based on the release of free oxygen radicals that activate terminal protein kinases, which are involved in the initiation of platelet apoptosis.<sup>10</sup>

The risk factors for hematological toxicity include the elderly, persons with renal insufficiency, hypoalbuminemia, those non-complying with dosing regimen of the drug or folic acid, and alcohol users. Cases of pancytopenia and thrombocytopenia have been described in patients with risk factors with low-dose methotrexate. Patients without risk factors are advised to monitor blood parameters once a week during the first month of methotrexate use and every two weeks during the second and third months. After the fourth month of therapy, in the absence of ADR, the frequency of blood tests can be reduced to every 2-3 months. It should be considered that 4 to 6 weeks after increasing the dose of methotrexate, the risk of hematologic ADR increases, and the patient's state should be closely monitored during this period. Since impaired renal function is one of the most serious predisposing factors for ADR, it is advised to measure the glomerular filtration rate in elderly patients and in those with reduced body weight, even if the blood creatinine and urea nitrogen values are normal. If a patient has impaired renal function. each subsequent methotrexate intake and dose increase should be preceded by test results that do not reveal any negative changes.

Patients taking methotrexate have a higher risk of interstitial pneumonia, pneumocystis pneumonia, and pulmonary fibrosis.<sup>6</sup> The phenomena of pulmonary toxicity have been observed in patients treated with both low and high doses of the drug, suggesting that the mechanism of toxicity is not conditioned by the methotrexate influence on folate metabolism only.11 The alleged and investigated mechanisms of the pulmonary toxicity of methotrexate are hypersensitivity reactions, direct cytotoxic effect of methotrexate on lung tissue, activation of mitogen-activated protein kinases, immunosuppression, and impaired cvtokine expression, causing an inflammatory response in lung tissues and destruction of lung tissue.12 Bronchoalveolar lavage histological and examination of the lung tissue confirm that the pathogenesis of lung injury is based on the hypersensitivity reaction.<sup>13</sup> Damage to the epithelium and manifestations of fibrosis suggest a direct cytotoxic mechanism of methotrexate effect.14

The toxic effect of methotrexate on renal function is a common ADR at high doses of the drug, but in rare cases methotrexate can cause kidney damage leading to kidney failure, even at low doses. Various mechanisms of low-dose methotrexate nephrotoxicity are assumed. Methotrexate has been established to cause renal tubular cell edema and necrosis, leading to irreversible damage to kidney tissue.<sup>15</sup> The drug is excreted primarily by the kidneys and being relatively insoluble in the acidic medium of urine, may have a direct toxic effect on the renal tubular epithelium or precipitate in the lumen, causing renal tubular intratubular obstruction. These processes result in a decreased glomerular filtration rate. Methotrexate causes damage to the cells of the renal glomeruli and renal tubules by increasing the oxidative stress the role of which has been identified in the pathogenesis of chronic kidney disease. The mechanism suggested is an increase in the markers of oxidative stress, 4hydroxynonenal and malonic aldehyde, with longterm use of low doses of methotrexate [16]. Another mechanism of methotrexate-induced alleged nephrotoxicity is decreased blood flow in the renal tissues and consequently impaired renal excretion of water and salts by the kidneys due to the increasing adenosine concentrations in the plasma and intercellular fluid and subsequent activation of adenosine receptors.<sup>17</sup>

Methotrexate affects the body's immune response and increases the risk of opportunistic infections. Cases of pneumocystis pneumonia, atypical actinomycosis, aspergillosis, cryptococcosis, meningitis and herpes virus infections, reactivation of tuberculosis, exacerbations of chronic hepatitis have been described with methotrexate treatment. Weekly low-dose methotrexate has been established to affect T cell activity<sup>18</sup>, however, it is suggested that an increased risk of infectious diseases may be caused by imbalance in the immune system due to chronic inflammation resulting from the underlying disease or the presence of concomitant disorders and comorbidities.

Methotrexate is prohibited in pregnant women due teratogenicity of the to the drug. Fetal malformations have been observed with methotrexate at all gestational ages, but the most pronounced teratogenic effect of methotrexate is observed during the first 6-8 weeks of pregnancy.<sup>19</sup> Methotrexate is also prohibited in lactating women because it is found in breast milk and can cause ADR in the baby. Oligospermia, a negative effect of methotrexate on spermatogenesis, has also been described in the literature.<sup>20</sup>

Methotrexate is a risk factor for the development of squamous cell carcinoma of the skin.<sup>21</sup> It has been found that long-term therapy with methotrexate is associated with the development of Epstein-Barr virus-associated lymphoproliferative diseases, which spontaneously regress after discontinuation of

methotrexate.<sup>22</sup> In addition, a study of the rate of malignancy risk increases has found that patients with rheumatoid arthritis treated with methotrexate were 50% more likely to have cancer compared to the general population, with five-fold increased risk of non-Hodgkin lymphomas and three-fold increased risk of melanoma and lung cancer.

ADR of mucositis, ulceration of psoriatic lesions, hyperpigmentation, alopecia, toxic epidermal necrolysis, nodulosis, and anaphylaxis have been described in patients taking methotrexate.<sup>23</sup> One of the skin ADR of the drug is methotrexate-induced nodulosis. It is assumed that the mechanism of formation of these giant cells is based on the methotrexate effect on the increase in adenosine synthesis and its interaction with adenosine A1 receptors.<sup>24</sup> Methotrexate-induced alopecia is thought to be caused by folate deficiency; it rarely occurs with low-dose methotrexate and resolves on own several months after its therapy discontinuation.

At the start of methotrexate therapy, some patients experience headaches, dizziness, weakness and emotional liability. One of the alleged mechanisms of methotrexate-induced neurotoxicity is the effect of increased release of adenosine and its accumulation in the central nervous system. The role of adenosine as a neurotransmitter and neuromodulator in the CNS has been experimentally confirmed: its increased accumulation is associated with the occurrence of headaches, nausea and somnolence. Adenosine has an inhibitory effect in the CNS: when binding to adenosine A1 receptors in the perifornical area of hypothalamus, adenosine can regulate the awakening and falling asleep processes, which may explain the weakness and somnolence that some patients experience after taking methotrexate.<sup>25</sup> In children treated with high doses of methotrexate, its neurotoxic effect was manifested in the pronounced somnolence and comatose state, which were reversible with theophylline therapy, a nonselective adenosine receptor antagonist. The neurotoxic effect of methotrexate may also be due to excitotoxic death of neurons, which can be caused by homocysteine metabolites: homocysteine acid and cysteine sulfonic acids.<sup>26</sup> Another possible mechanism may be impaired metabolism of biopterin, leading to a synthesis of decrease in the monoamine neurotransmitters.27

Rarely, low doses of methotrexate cause osteopathies like bone pain, long bone fractures, and osteoporosis.

Methotrexate-induced osteopathy syndrome was first described as a stress fracture of the lower extremity bones, diffuse bone pain, and osteoporosis in children with acute lymphoblastic leukemia receiving long-term therapy with low-dose methotrexate. Several cases of methotrexateinduced osteopathy in patients with rheumatoid arthritis and psoriasis have been described. An animal study has found that long-term use of lowdose methotrexate causes pronounced osteopenia by reducing osteoblast activity and increasing osteoclast activity.<sup>28</sup>

It should be considered that in some cases, even a single dose of methotrexate may lead to serious and complex ADR. The risk of fatal ADR with methotrexate therapy is small. The toxic effects of methotrexate on the hematopoietic system, respiratory system and liver are most life threatening. Therefore, careful identification of risk factors for increased toxicity of methotrexate and comprehensive monitoring of the patient's condition with regard to these ADR groups is necessary. Hepatologic and hematologic ADR of methotrexate may manifest as weakness, nausea, stomatitis, and syncope in patients. Similar symptoms that develop during methotrexate therapy should be alerted. Careful monitoring of the patient's condition will reduce the risk of ADR. Caution should be exercised in patients with hepatitis, hepatic cirrhosis, and other conditions associated with impaired hepatic function due to its potential hepatotoxicity. Liver parameters should be closely monitored in these patients.

Despite the lack of unambiguous data regarding the complete or partial prohibition on alcohol consumption in the period of methotrexate therapy, history of alcoholism and alcohol-induced liver diseases are relative contraindications to the drug administration. The use of methotrexate may be restricted by administration of other drugs that have toxic effects on the liver. Since the drug is primarily excreted by the kidneys, methotrexate should be used with caution in patients with renal impairment. With impaired renal excretion of methotrexate, plasma concentrations of the drug increase and therefore the risk of its toxicity increases. Close attention should be paid to the state of patients with immunosuppression and chronic infections prone to exacerbation as a result of immunosuppressive effect of methotrexate. In exacerbation of the infectious process, the drug should be temporarily discontinued. Before prescribing methotrexate, it is necessary to assess whether the patient is able to fulfil all prescriptions responsibly, since the therapy success and patient's safety depend largely on careful selection of the dose regimen and duration of therapy, as well as on regular examination for potential ADR.

Often, a potential benefit of therapy may outweigh the possible risks for a patient with a disease or condition that limits the use of methotrexate. Treatment decisions should be made by the physician individually for each patient based on the risk-benefit assessment.

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### The Importance of Telemedicine in a Post COVID World

BHUPESH SHARMA<sup>1</sup>, SANJANA MANOCHA\*1, NYAGAM YANGZOM<sup>2</sup>

Telemedicine has found immense popularity, especially in a COVID-19 affected world. Its application shall improve the quality of health care provided to patients and help in time management as it help facilitates optimized referral systems which are based on the immediate/follow up needs of the patient, decision-making, reduction in patient's waiting time as well as consultation time. This review is an effort to shed light on the main practical applications of teledentistry for emphasizing potentialities, problems, and applications of this relatively new branch in medicine. The paper also highlighted highlight the various aspects of telemedicine in relation to the healthcare sector, its advantages/disadvantages in a post COVID-19 world.

KEYWORDS: Telemedicine, Artificial Intelligence, Technology

### INTRODUCTION

The healthcare sector in an ever-evolving branch. A particular advancement in this sector is the "telemedicine". which has help facilitate immediate/short-term and long-term care of the patient. An advantage of this is that health information is communicate between practitioners and the patient through e-mail and interactive chats or videoconferences, which increasing convenience for the patient and reduces the need to physically visit the doctor's clinic. This is especially helpful in remote areas where provision of immediate and urgent care would not be possible.1

The use of telemedicine is believed to improve the quality of health care provided to patients and help in time management as it help facilitates optimized referral systems which are based on the immediate/follow up needs of the patient, decision-making, reduction in patient's waiting time as well as consultation time. Another added advantage is that telemedicine can be used for peer education and consultations, case discussions among their peers and colleagues.<sup>2</sup>

The entire process of networking, sharing digital information, distant consultations, workup, and analysis is dealt with by a segment of the science of telemedicine and this review paper aims to highlight the various aspects of telemedicine in relation to the healthcare sector, its advantages/disadvantages in a post COVID-19 world.<sup>3,4</sup>

### HISTORY

The first published instance documenting the use of telemedicine occurred in the early 20<sup>th</sup> century when electrocardiograph data were transmitted through telephone wires.<sup>5</sup> In its modern from, telemedicine started in the 1960s, primarily driven by the innovations in military and space sectors, coupled with the expertise of a few individuals who were using readily available commercial equipment.<sup>6</sup> Examples of early technological milestones in telemedicine include the use of television to facilitate consultations between specialists at a psychiatric institute and general practitioners at a state mental hospital<sup>7</sup>, and the provision of expert medical advice from a major teaching hospital to an airport medical centre.<sup>8</sup>

The introduction and popularization of internet has further accelerated the pace of telemedicine, which, in turn expanded its scope and now includes various webased applications (e.g. e-mail, teleconsultations and conferences applications) and multimedia approaches (e.g. digital imagery and video). In addition, in a post COVID world, the use of various teleconsultations is on the rise.

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### **INTRUMENTS REQUIRED**

In most cases, the primary requirement is of having a stable, high speed internet capable of uploading patient record files quickly. The second major requirement is of having an internet enabled device with camera which needs to be used for communication, modern smartphones and laptops are quite capable of doing so. It is desired that the conversation be encrypted and kept confidential. Also, the uploaded files of the patient need to be maintained on a secure and private server.

There is also a need for a person to be well-versed with operation of such devices. Among the illiterate and old aged people, at times, there might a need for an internet and app savvy person to connect the person with the server.

### **DEFINITION OF TELEMEDICINE**

As per the WHO, telemedicine is defined as the following though this broad description:

"The delivery of health care services, where distance is a critical factor, by all health care professionals using information and communication technologies for the exchange of valid information for diagnosis, treatment and prevention of disease and injuries, research and evaluation, and for the continuing education of health care providers, all in the interests of advancing the health of individuals and their communities".9

### TELEMEDICINE IN EMERGENCY CASES AND TRIAGE

In a post COVID-word, hospitals need to be everprepared to handle any emergency/ efficiently perform patient triage. This can be achieved only by improving the efficiency of emergency departments, without compromising on patient care; and telemedicine comes as a boon in such instances. It allows for remote and ambulatory monitoring of patients as well as help undergo remote triage and assessment of emergencies including, but not limited to MI, fractures bones, trauma, etc.<sup>10</sup>

The inclusion of automated forward triage systems that use algorithms to categorize patients into risk groups could also be utilized and same time of emergency respondents and physicians.

### TELEMEDICINE AND ITS APPLICATION IN LONG-TERM CARE FACILITIES

As discussed above, the use of smartphones, tablets and other internet devices among seniors remains quite low. A recent study in the year 2019 revealed that only 21% of the residents in retirement homes used the internet and among those, 13% used a smartphone, and 5% used a tablet.<sup>11</sup> It has been reported that internetbased device adoption is associated with the living environment, individual characteristics, functional health, chronological age, education, and technology interest of a person and is directly related to technology adoption among the oldest age groups.<sup>12</sup>

### ARTIFICIAL INTELLIGENCE ASSISTED TELEMEDICINE

The use of innovative data-driven Artificial Intelligence (AI) algorithms shall apply machine learning to large datasets of disease populations and provide accurate results. An important fact is that these models can learn directly from data without any prior statistical modelling, thus producing more objective results while focusing on prediction generalizability for diagnostic purposes on diverse populations. Ever since the COVID-19 pandemic outbreak, AI has been used for international efforts for COVID-19 forecasting, prevention and treatment by using data-driven tools and pooled datasets from across the globe.<sup>13,14</sup>

An added of advantage of the Machine Learning (ML) model is that it incorporates an important analysis that helps develop cost-effective protocols. Such datadriven computational approaches can test for synergistic variable combinations and elimination of redundancy enables more effective diagnosis of patients under the purview of telemedicine.<sup>15</sup>

### LEGAL AND PRIVACY ISSUES/RESOLUTIONS

There are a few legal and privacy issues pertaining to telemedicine and they are as follows:<sup>16</sup>

**a). Liability:** Despite its numerous advantages, there is the possibility that a patient may perceive this method as inferior because the consulting professional does not perform a hands-on examination and hence would not be able to reach an accurate diagnosis. A major issue including liability is when information

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provided over the telephone is misinterpreted by either the patient or the attending physician.<sup>17</sup>

**b). Reimbursement and Licensure:** Unfortunately, there have been incidents in which practitioners who were eligible for reimbursement were unhappy with either the payments made, or due to delayed payments made to them. In addition, healthcare professionals are only licensed to practice within certain jurisdictions, and telemedicine requires multiprovince licensure, which might lead to legal issues both for the service provider and the physician. For physicians, applying for applications for practising license in different provinces/states can be lengthy and expensive process.

c). Privacy and Confidentiality: Telemedicine should ensure that privacy, security, and confidentiality of data of patients must be maintained at all times and only authorized users-those who directly involved in the ongoing care and treatment of a patient—and only those having a legal right can approach the systems to servers.18 It is important that nurses and other healthcare professionals need to be mindful of these issues, especially when technicians not bound by professional codes of ethics are present at telemedicine sessions.1

**d). Quality:** Internet speed; and access to information at any time, from any place, are essential to maintaining a high quality of service; slowdowns or outages in service are not acceptable; especially during emergency situations or where immediate triage is necessary. The scientific literature has reported inadequate funds among various establishments for maintenance of the technological infrastructure.<sup>19</sup>

### **CONCLUSION**

In a post COVID world, there is no doubt that telemedicine will grow manifold and people will enjoy the benefits offered it. However, one needs to be cautious of its drawbacks provide evidence based guidelines on a timely basis for the efficient use of this technology.

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### Assessment of Sleep Habits and Quality of Sleep among Elderly Residing in Rural Areas of Patiala: A **Community-Based Cross-Sectional Survey**



### YASHIKA KAUSHAL<sup>\*1</sup>, RATIBHA KAUSHAL<sup>2</sup>, ISHA SHARMA<sup>3</sup>, SHEENAB MITTAL<sup>4</sup>

INTRODUCTION: Among the elderly, sleep problems are quite prevalent and can lead to many adverse health consequences.

- AIM: To assess the quality of sleep among the elderly residing in rural population and factors related to it, and provide necessary recommendations for its Α prevention.
- MATERIALS AND METHOD: In this cross-sectional study, elderly aged above 60 years residing in Patiala were taken and were interviewed separately B
- using the modified version of the Pittsburgh Sleep Quality Index (PSQI), which was pre-tested and pre-validated prior to commencement of the study. Data
- S recorded was divided into seven components and each component had an individual range of o (no difficulty) to 3 (severe difficulty) points and added to obtain a combined score of the individual with a range of o(no difficulty)-21(severe difficulty) points. Based on the combined score, elderly obtaining a Т total score of 5 or greater was classified as having "poor sleep quality". Statistics were applied using SPSS version 22.0, using the student's t- test, and
- multivariate analysis. A p value < 0.05 was considered as significant. R
- RESULTS: Out of 108 elderly people, most of the participants (62.9%) belonged to the age group of 60-75 years, out of which the majority (65.7%) were
- males. Most elderly reported having "fairly good" subjective sleep quality (53.7%, p=0.01) and was found to be significant with a global PQSI score of 7.22±4.31. Multivariate analysis revealed that significant "poor sleep quality" was observed in elderly aged above 75 years (OR:1.25, p=0.01) followed by elderly A С
  - who were Immobilized (wheelchair/Bed ridden) (OR: 1.87, p=0.01).

CONCLUSION: Efforts should be directed towards proper education of not only the elderly, but their children as well as colleagues and guardians to Т improve the sleep score of the elderly population.

### **KEYWORDS:** Sleep, Elderly, Insomnia

### **INTRODUCTION**

In a human being's life, sleep is an unavoidable dailyrequired activity and is a highly significant factor contributing to one's overall health.<sup>1</sup> Sleep has a positive effect on quality of life, body functions and homeostasis.<sup>1</sup> deficiency can lead to the weakening of Its immunological functions, poor general well-being and psychiatric illnesses, especially among the elderly population.<sup>2</sup>

Statistics from a global study featuring the sleep profiles of 48 countries revealed that not even a single country manages an average of 8 hours of sleep/night among its residents with the worst sleepers being reported from Japan, Saudi Arabia, Sweden, India and Philippines.<sup>3</sup>

Sleep deprivation is defined as getting inadequate sleep, i.e. less than 7-9 hours per day.4 Apart from sleep deprivation, Poor sleep quality includes sleep latency, restless sleep and insomnia.5 Experiments in sleep deprivation among volunteers have shown that a sleepdeprived person is incapable of sustaining normal levels of efficiency, both physically and mentally.<sup>6</sup>

Among elderly, a good quality of sleep is essential for their health, as its deprivation is linked to various diseases. As the inability to sleep can result in a negative impact leading to attention problems, delayed response time, inability to concentrate, forgetfulness, increased risk of falls, decreased performance in daily life activities and increased risk to develop depression and anxiety.7

Since the elderly are at a greater risk of the consequences of poor sleep, the present study was an attempt to assess the quality of sleep among the elderly residing in rural population in Patiala, Punjab, India and factors related to it, and provide necessary recommendations for its prevention.

### **MATERIALS AND METHOD**

The present study was designed to be cross-sectional in nature, and was conducted among the elderly (60 years and above) residing in Patiala, Punjab, India. Post ethical clearance and obtaining all necessary approvals, the study was conducted for a period of five months i.e. from 1<sup>st</sup> March, 2018 to 31<sup>st</sup> July, 2018. Since, elderly were

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contacted by the researchers, the study adopted a convenience sampling. The elderly were recruited using a combination of house to house surveys, by visiting old age homes and referral by already recruited elders (Snowball sampling). All the elderly residing in one household were taken and were interviewed separately to preserve the confidentiality of data. Data was collected by primarily using the Pittsburgh Sleep Quality Index (PSQI) and adopting it as per the needs of the present study. The questionnaire was then pre-tested and pre-validated.<sup>8</sup> The elderly were educated regarding the aims and objectives of the study and a written consent was taken from them prior to the conduct of the study.

**Inclusion criteria:** Elderly above 60 years; the data recorded was divided into seven components: subjective sleep quality (C1), sleep latency (C2), sleep duration (C3), habitual sleep efficiency (C4), sleep disturbances (C5), use of sleeping medications (C6) and daytime dysfunction (C7) over the last month. Each component has an individual range of 0 (no difficulty) to 3 (severe difficulty) points. Responses of all seven components were added to obtain a combined score of the individual [range of 0(no difficulty)-21(severe difficulty) points]. Based on the combined score, elderly obtaining a total score of 5 or greater was classified as having a "poor sleep quality".<sup>8</sup>

**Exclusion criteria:** Elderly not present during the day of the study (due to any reason) and those who did not provide consent.

Data was collected and entered into Microsoft excel and descriptive statistics were applied. Inferential statistics were applied using SPSS version 22.0,<sup>9</sup> by using the student's t- test, and multivariate analysis. A p value < 0.05 was considered as significant.

### RESULTS

Table 1 depicts that out of 108 elderly people, most of the participants (62.9%) belonged to the age group of 60-75 years, out of which the majority (65.7%) were males. 81.4% of the elderly people were still married while 1.9% were never married. Unfortunately, 45.4% of the elderly reported irregular physical activity, and 8.3% were immobilized. 47.2% of the elderly were found to be smokers.

The classification of the elderly as per the components of the PSQI is depicted in table 2. Most elderly reported having "fairly good" subjective sleep quality (53.7%, p=0.01) and was found to be significant. Another significant observation was that the habitual sleep

SOCIODEMOGRAPHIC	FREQUENCY	
VARIABLES	(%)	
AGE ( in years)		
60-75	68 (62.9)	
>76	40 (37.1)	
GENDER		
Male	71 (65.7)	
Female	37 (34.3)	
MARITAL STATUS		
Still Married	88 (81.4)	
Widowed/widower	18 (16.7)	
Never Married	02 (1.9)	
PHYSICAL ACTIVITY		
STATUS		
Regular	50 (46.3)	
Irregular	49 (45.4)	
Immobilized (wheelchair/Bed	9 (8.3)	
ridden)		
SMOKING STATUS		
Smokers	51 (47.2)	
Non-Smokers	57 (52.8)	
<b>Table 1.</b> Sociodemographic and behavioural           characteristics of study participants		

efficiency of >85% was observed in 80.5% of the elderly (p=0.04). It was also observed that 88.8% did not take any sleep medication since the last month. Significant PQSI scores of >5 indicating poor sleep quality was observed in 63.9% of the elderly (p=0.02).

A multivariate analysis of sleep quality (PSQI) and associated factors among the elderly (Table 3), it was observed that significant "poor sleep quality" was observed in elderly aged above 75 years (OR:1.25, p=0.01) followed by elderly who were immobilized (wheelchair/bed ridden) (OR: 1.87, p=0.01).

### DISCUSSION

The present study, although descriptive in design, has provided significant insights into the sleeping habits of the 63.9% elderly of Patiala, Punjab, India. These scores are similar to the findings of Chaudhary et al.  $(2020)^2$ , but lower as compared to 72.4% reported by George et al.<sup>7</sup> among elderly in rural Kerela India. These figures are quite alarming and demand immediate attention (Panda et al.)<sup>10</sup>, among healthy South Indian population aged 35.1±8.7 years who reported good-quality sleep with a global PSQI score of  $\leq$ 5 among 93.8% of the population. Such discrepancies in the PQSI scores among adults and

COMPONENTS OF PSQI	FREQU	p- VALUE					
Subjective Sleep Quality							
Very Good							
Fairly Good		8 (53.7)	0.01*				
Fairly Bad		5 (14.8)					
Very Bad		7 (6.5)					
Sleep Latency (in minutes)							
<15 minutes	18	8 (16.7)					
16-30 minutes		9 (36.1)	0.78				
31-60 minutes		2 (20.4)					
>60 minutes	29	9 (26.8)					
Sleep D	<b>uration</b> (i	in hours)					
>7 hours	28	8 (25.9)					
6-7 hours		9 (45.4)	0.065				
5-6 hours		2 (11.1)	-				
<5 hours	10	9 (17.6)					
Habitu	al Sleep E	fficiency					
>85%	8	7 (80.5)					
75-84%		4 (12.9)	0.04*				
65-74%		5 (5.5)					
<65%		1 (1.1)					
Use of	Sleep Me						
Not during the past							
month	,	5 (88.8)					
Less than once a	:	3 (2.8)	0.89				
week							
Once or twice a week	(	6 (5.6)					
Three or more time a	1	3 (2.8)					
week							
	ime Dysft	inction					
Not difficult		9 (71.8)					
Little difficult	15 (15.6)		0.06				
Difficult	7 (7.2)						
Very difficult	5 (5.2)						
	p Disturb	ances 2 (2)					
Not in last month							
Once in a week	81 (75.0)						
1-2 times a week	13 (12.1)		0.77				
More than thrice a	14 (12.9)						
	week Total PSQI score of Study Participants						
Total PSQI sco	ore of Stu		S				
		GLOBAL					
		PQSI					
		SCORE (MEAN ±	0.5-*				
Loca then -	6-	`	0.02*				
Less than 5 More than 5	69	SD)					
More than 5	(63.9)	7.22±4.31					
Table 2. Distribution of respondents according to							
components of Pittsburgh Sleep Quality Index (PSQI)							

elderly focus on the need for promoting good sleep habits among the elderly through proper screening for

ASSOCIATED FACTORS	OR (95% CI)	P- VALUE		
Age (in years)				
60-75	1.32 (0.74-12.25)	0.90		
>76	1.35 (0.55-15.58)	0.01*		
Widow	0.22 (0.14-1.95)	0.55		
Immobilized	1.87 (0.56-20.68)	0.01*		
(wheelchair/Bed ridden)				
Smokers	1.88 (1.47-21.75)	0.06		
Table 3. Multivariate analysis of sleep quality (PSQI)         and associated factors				

potential factors disturbing their sleep patterns. The global PQSI score of the elderly in the present study was found to be  $7.22\pm4.31$ , which is lower as compared to George et al. ( $8.04\pm4.59$ )<sup>7</sup> and lower in comparison to Das et al.<sup>11</sup> (Higher IQR of GPQSI scores in population aged >70 years). As reported by Farazdaq et al.,<sup>12</sup> a few factors associated with an increased risk of poor sleep quality among elderly included aging, divorce, being widowed, caffeine consumption, cigarette smoking 2 hours before bedtime coupled with co-morbidities such as GERD and depression to name a few.

As per results of Wu et al.<sup>13</sup> higher level of physical activity was associated with better sleep quality among elderly population in Taipei while independently considering physical influence on sleep. As per results of the present study, 45.4% of the elderly had irregular physical activity while 8.3% were immobilized and hence, could not do any physical activity. This could be the reason for such poor sleep scores in the elderly studied in the present study. In addition, Razali et al.<sup>14</sup> reported that sleep quality was associated with age the same can be seen with the results of the present study.

The limitations of the study include social desirability bias by the respondents or recall bias(in some instances). In addition, data as coded and the interviewers were duly standardized to eliminate interviewer's bias. Due to such measures, the authors conclude that the results of the present study can be generalized for the Indian population and can be used for comparison between global elderly population.

### CONCLUSION

Based on the results of the present study, the sleep scores of the elderly were high and efforts should be directed towards proper education of not only the elderly, but their children as well as colleagues and guardians through proper community education programmes so that efforts could be directed towards improving the sleep score of the elderly population.

### DISCUSSION

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