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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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Editorial

TRANSLATIONAL RESEARCH: THE NEED OF TIME

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ABSTRACT
Translational research, is an innovative and multidisciplinary approach to bring laboratory findings into clinical practice or explain clinical findings in the laboratory settings. This primarily bridges the gap between basic scientific research and the clinical applications. It focuses on transforming discoveries made in the laboratory into practical applications to improve human health. For a number of decades most of the research funds were utilized for basic research thus a lot of knowledge is produced without clinical application. Thus it's now time to focus on translational work so that all the knowledge produce should have practical applications. This may give new diagnostic tests, identifies novel therapeutic targets planting a seed for development of new therapeutic molecules. This editorial presents a brief of the reasons to focus on translational research in countries like Pakistan.

Key Words: Translational Research, Medical Research, Basic Research

INTRODUCTION

Translational research, is an innovative and multidisciplinary approach to bring laboratory findings into clinical practice or explain clinical findings in the laboratory settings. This primarily bridges the gap between basic scientific research and the clinical applications. It focuses on transforming discoveries made in the laboratory into practical applications to improve human health. For a number of decades most of the research funds were utilized for basic research thus a lot of knowledge is produced without clinical application. Thus it's now time to focus on translational work so that all the knowledge produce should have practical applications. This may give new diagnostic tests, identifies novel therapeutic targets planting a seed for development of new therapeutic molecules. This editorial presents a brief of the reasons to focus on translational research in countries like Pakistan.

Bringing basic and clinical research together

Basic research focuses on topics related to fields like genetics, immunology, and pharmacology, such as studying genetic mutations found in a disease or looking at molecular structure of medicinal plant extracts without exploring its use in clinic, this has wasted lot of money, energy and resources. Thus adding translational research aspect in all basic science discoveries such looking at genetic mutations in a disease and correlating it with clinical findings or clinical outcome can potentially result in the development of diagnostic or prognostic tests. Thus, this will act as a bridge, facilitating the translation of scientific knowledge into tangible patient benefits.

Medical research advancement

Putting basic and clinical research into different corners and when to bring them into practice would take decades. In contrast putting translational aspect in basic research project will expedite the

process, ensuring that innovative treatments and therapies developed and made available to patients more quickly. This will enhance medical discoveries and solve medical health issues more quickly. Given the emerging infectious diseases and rising trend of chronic illnesses it is need of time to have translational component in each medical research theme.

Provide foundation for precision medicine

Precision medicine takes genomics, proteomics and all -omics involved in human body to provide tailored medicine for each individual. Thus translational research plays fundamental role in development of precision medicine concepts. This will significantly reduce number of failure of therapy, its side effects thus improve clinical outcome.

Multidisciplinary approach

The fundamental aspect of the translational research is multidisciplinary approach. All basic and clinical research departments have their contribution. This without any doubt fosters collaboration among key stakeholders of healthcare system including basic scientists, clinical practitioners and pharmaceutical industry. This collaboration is essential to ensure the utilization of scientific discoveries into clinical practice, and resulting in safe and effective therapeutic options.

Targeting Unmet Medical Needs

The pattern of new emerging diseases is alarming in medical sciences. Moreover, there are a number of diseases for which treatment is still a dilemma. Translational research has strength to explore new avenues for tackling these issues and attempting to answer these questions. This aspect not only helps in improving healthcare system by providing proper evidence based diagnosis and treatment but also boost economy by reducing treatment expenditure and improving clinical outcome.

Streamlining Drug Development

The pharmaceutical industry benefits greatly from translational research. By incorporating translational approaches in drug development. Researchers can identify potential candidates more efficiently, understanding their mechanisms of action, and assess their safety and efficacy. This leads to faster drug development and approval, ultimately benefiting patients.

Health Economics

Translational research has the potential to reduce healthcare costs by minimizing the time and resources needed to develop new treatments. This can result in more affordable healthcare solutions and greater accessibility to effective treatments.

Improving Public Health

By addressing health issues at their root through translational research, public health can be significantly improved. For instance, research into lifestyle interventions, preventive measures, and early diagnostics can reduce the prevalence of chronic diseases and the associated burden on healthcare systems.

CONCLUSION

Translational research is the need of the time for various reasons. It not only bridges the gap between scientific discoveries and patient care but also accelerates medical progress, promotes collaborations, targets unmet medical needs, streamlines drug development, has economic benefits, and, most importantly, improves public health. By investing in translational research, we can ensure that scientific knowledge is effectively translated into clinical practice, resulting in better patient outcomes and a healthier society. It is a crucial approach that should be further supported and promoted to meet the evolving healthcare challenges of our time.

Research article

ASSESSMENT OF ANTI-MALARIAL POTENTIAL OF ALLIUM SATIVUM AGAINST PLASMODIUM VIVAX

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ABSTRACT

Malaria is a vector-borne protozoal disease, caused by genus Plasmodium, where female anopheles' mosquito works as a vector to transfer malarial parasite. The disease has been reported to be endemic in tropical and subtropical regions of the world. Since drug resistance of the Plasmodium species and economic burden of the disease are the major concerns associated with malaria. Thus, most of the world's population is focusing on the utilization of medicinal plants as the natural treatment for several diseases including malaria. There is limited published data available regarding anti-malarial activity of Allium sativum against Plasmodium vivax. Therefore, this study was aimed to assess the in-vitro anti-malarial activity of Allium sativum methanolic extract. The methanolic extract of Allium sativum showed significant anti-plasmodial activity (80.57%) at 0.2 mg/ml highest tested dose after 24h. The phytochemical analysis showed the presence of Flavonoids, Vinyldithiins, Ajoenes, Alliin and Allicin in the Allium sativum methanolic extract. Among the phytochemicals, only Allicin at the highest tested dose (0.2mg/ml) showed the inhibition (59.75%) of P. vivax inhibition. Allium sativum methanolic extract exhibits anti-plasmodial activities in-vitro. However, further studies are required to assess the in-vivo anti-plasmodial activity of Allium sativum methanolic extract against plasmodium vivax in future.

Key Words: Plasmodium vivax, Allium sativum¸ Parasite, Antimalarial activity, methanolic extract, in vitro.

INTRODUCTION

Malaria is a vector-borne parasitic infection, caused by intra-erythrocytic protozoa parasites of the genus Plasmodium (P). Female Anopheles mosquito transmits the parasites that can cause malaria. Malaria is mostly reported as endemic in tropical and subtropical regions of the world. Malaria affects over half of the global population(1). More than 100 known Plasmodium species have been reported around the globe, however, only five of these species including P. vivax, P. malariae, P. knowlesi, P. falciparum and P. ovale are known to significantly infect human(2). Due to Pakistan's strategic location in a geographical area where more than 60% of its population has been reported positive for Malaria. In Pakistan, Plasmodium vivax can cause about 64% of malarial cases(3). After the Second World War, the struggle to control malaria was intensively promoted(4). Millions of population is at risk of malaria but it is considered as neglected disease in the tropical regions(5). According to a recent survey in 2014, 1.2 billion people have been reported to be at high risk of malaria. Remarkably, malaria cases occur more frequently in high-risk zones, affecting 97 nations and territories, with 712,000 deaths recorded in the African region(3). Due to the drug resistance of malarial parasites, the available medicines have low effect on overcoming the Plasmodium species. The cost of the current medicines available at markets are difficult to manage in poor countries where lifestyles are below the standard level. Therefore, new medicines are required to overcome drug resistance issue.

Eighty percent of the world's population now relies on plants as the natural medicines as the main source of healthcare therapy(6). Recently, the use of antibiotics and the majority of synthetic medications have been constrained due to disagreeable side effects on the growth of pathogenic bacteria that are resistant to these drugs, hazardous side effects, and withdrawal problems(7). To avoid such problems, the scientific world is now focusing on the traditional ways of treatment utilizing medicinal plants and their derivatives. For the treatment of numerous vector-borne diseases, including malaria, majority of the world's population is now mainly focusing on the use of herbs and plants as their daily alternative medicine(8). For several decades, medicinal plants are in continuous use to treat human diseases including stomach pain, headaches, diabetes, hyperacidity, viral infections, bacterial infection, protozoan infections, and many others.

Garlic (Allium sativum L.; Family: Amaryllidaceae) is an annual aromatic herbaceous plant. It is one of the earliest and most significant plants that have been utilized to use traditional medicine since ancient times (9,10). It is regarded as the second most widely used species of Allium family after onion (Allium cepa L.), which is used as a treatment for a number of common diseases like the common cold, the flu, snakebites, and hypertension(11). According to research conducted on humans, Allium species and their active ingredients have been shown to lower the risk of diabetes and cardiovascular disease, defend against infections by boosting the immune system, and have antibacterial, antifungal, anti-aging, and anti-cancer capabilities(12). Allium sativum contains various medical properties and elements, which can be utilized for various life purposes including treating several diseases(13). Somehow, limited pieces of information are available on the antimalarial activities of Allium sativum against P. vivax. Therefore, this study was aimed to assess the *in-vitro* anti-malarial effects of Allium sativum methanolic extract against P. vivax.

METHODS

Plant collection and Preparation of garlic extract

Fresh cloves of garlic were collected at the natural environment in the western-south areas of district Bannu, Khyber Pakhtunkhwa, Pakistan with coordinates (latitude: 32.986111 and longitude: 70.604164). After washing with distilled water, methanolic extraction was performed according to the published method as discussed earlier(14), with slight modifications. The garlic cloves were grinded and plant extract was prepared by mixing 20 mg of ground garlic with 100 ml of methanol in a graduated cylinder. Before being filtered with 11µm grade cellulose filter paper, the suspension was shaken in an electric shaker for 24 hours at 28°C. The final filtered solution was placed into multiple containers for freeze-drying after the filtration procedure was repeated twice. The final product (200 g) of freeze-dried garlic powder was kept at 4°C for further processing.

Phytochemicals analysis

The phytochemical analysis of Allium sativum was performed according to previously published protocol with slight modifications for the presence of medically important phytochemicals(15).

Identification of Plasmodium vivax through Microscope

Thin blood smears were made from the collected blood samples and observed under Light Microscope (100X) magnification lens for the presence of P. vivax.

Culturing of Plasmodium vivax

Plasmodium vivax strains were cultured at the Molecular Laboratory in the Department of Zoology University of Science and Technology Bannu, Khyber Pakhtunkhwa, Pakistan in a candle jar. For culturing, a blood medium mixture of 200 µl having 2.0% hematocrit, in a liquid sterile McCoy's 5A medium provided with human serum 20%, was used. The plasmodium strains were cultivated in a glass jar and kept on incubation at 37 °C. At around 40% of the adult schizont ring stage, the incubation was completed. The culture was supplied with Gentamicin sulfate (5 µl). Thin blood smears stained with 5% Giemsa stain were prepared and observed under microscope. In order to propagate the culture the infected red blood cells were further used for inoculation in a fresh medium(16).

In vitro anti-plasmodial activity

The plant extract and phytochemicals were tested for their in vitro anti-plasmodial activity in as previously reported (17). The anti-protozoan activity was carried out in 90 microplates. The positive controls utilized were Chloroquine and Nevaquine, whereas the negative controls employed parasitized culture on microplates without the use of any medicine or plant extract. Six different concentrations (0.02, 0.04, 0.06, 0.08, 0.10, and 0.2 mg/ml) of plant extract, phytochemicals, and drugs were used as reported earlier (18,19). The concentration of CO2 was increased by gently shaking the microplates in a candle jar. For 24 hours, the plates were kept at 37°C in an incubator. After 24 hours, each microplate's supernatant was discarded, and red blood cells were extracted using a micropipette to create thin smears that were stained with the Giemsa dye and examined under a microscope as given in Figure 1.

Statistical analysis

The percentage of maturation and inhibition was calculated by using the following formula:

Inhibition(%)= No. of developed schizonts in experimental group x 100 / No. of developed schizonts in control group

Maturation (%)=100 – Inhibition %

RESULTS

Phytochemicals analysis of Allium sativum

The phytochemicals analysis was performed and showed the presence of Alliin, Allicin, Ajoenes, Vinyldithiins and Flavonoids in Allium sativum methanolic extract given in Table 1. Our data is correlated with the already published report(20). Herein our data suggest that due to presence of various compounds could modulate the fast growth of P. vivax over RBC of humans.

Anti-plasmodial potential of Allium sativum

Next we examined the anti-plasmodial potential of Allium sativum extract by comparing with slandered anti-malarial drugs concentration LD50 0.082 mg/ml such as Nevaquine and Chloroquine. The in-vitro anti-plasmodial potential of A. sativum extract was analogous and comparable to Chloroquine and Nevaquine as shown in Table 2. The methanolic extract of A. sativum showed maximum 80.57% inhibition of P vivax at 0.2 (mg/ml) tested dose.

By comparing the Anti-plasmodial activity of different phytochemicals present in Garlic (Allium sativum) with control group such as Chloroquine on Plasmodium vivax.

The phytochemicals were tested for the inhibition among which only Allicin at the highest tested dose (0.2 mg/ml) exhibited 59.75% growth of P. vivax, which was almost analogues and comparable to Chloroquine as shown in Table 3.

Table 1: Represents the photochemical constituents of Garlic (Allium sativum) in methanolic extract

S. No.	Phytochemicals	Methanolic crude extract
1	Allicin	+
2	Alliin	+
3	Ajoenes	+
4	Vinyldithiins	+
5	Flavonoids	+

Figure 1: Represents the anti-malarial effects of Allum sativum on Schizonts of P. vivax using Microscopic Examination

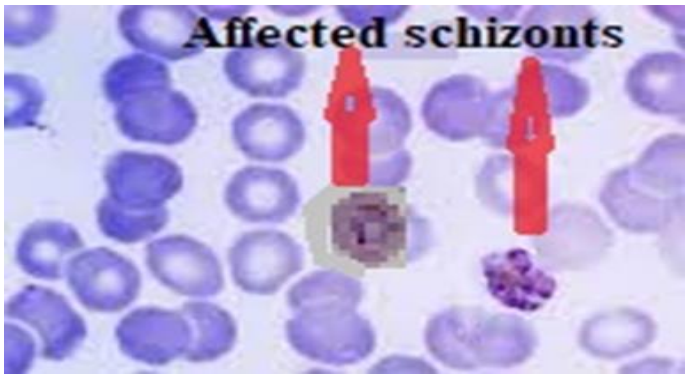

Table 2: Represents the in-vitro activity of the extract on Plasmodium vivax.

Extract/drugs	Concentration (mg/ml)	Schizonts in experimental group (mean ± SD)	Schizonts developed in control group (mean)	Maturation %	Inhibition %	LD50 mg/ml
Allium sativum	0.02	184.44 ± 1.22	258.44	71.36	28.64	0.082
	0.04	180.44 ± 1.22	258.44	69.81	32.19	
	0.06	159.22 ± 1.21	258.44	61.60	38.4	
	0.08	140.22 ± 1.19	258.44	54.25	45.75	
	0.10	93.44 ± 2.98	258.44	36.15	63.84	
	0.2	50.22 ± 2.82	258.44	19.43	80.57	
Chloroquine	0.02	100.67 ±1.70	258.44	40.11	59.89	0.070
	0.04	80.74 ± 1.79	258.44	31.24	68.76	
	0.06	62.89 ± 2.87	258.44	25.20	75.8	
	0.08	35.44 ± 2.90	258.44	13.71	86.29	
	0.10	27.11 ± 2.43	258.44	12.83	87.17	
	0.2	13.00 ± 2.42	258.44	5.03	94.48	
Nevaquine	0.02	124.67 ± 1.76	258.44	48.23	51.77	0.077
	0.04	104.67 ± 1.69	258.44	40.50	59.32	
	0.06	79.31 ± 0.89	258.44	30.68	69.32	
	0.08	59.33 ± 2.41	258.44	22.95	77.05	
	0.10	27.60 ± 0.79	258.44	10.67	89.33	
	0.2	**13.22 ± 0.89**	**258.44**	**5.11**	**93.89**	

Table 3. Shows the in-vitro anti-plasmodial activity of different Phytochemicals of Garlic (Allium sativum) methanolic extract on Plasmodium vivax

Concentration (mg/ ml)	Inhibition percentage					
	Chloroquine	Allicin	Alliin	Ajoenes	Vinyldithiins	Flavonoids
0.02	62.76	26.76	2.50	2.05	1.08	2.10
0.04	64.76	30.76	3.07	2.20	1.15	2.20
0.06	67.8	34.8	4.03	2.90	1.30	2.35
0.08	75.1	41.1	6.06	3.12	1.45	2.50
0.10	83.17	48.17	8.07	3.25	1.93	2.75
0.2	90.75	59.75	11.10	4.12	2.42	2.95

DISCUSSION

Over long periods, the world has been focusing on the use of medicinal plant remedies as a natural treatment for several infectious diseases. Due to the advancement in research activities on medicinal plants, many different kinds of anti-plasmodial drugs have been discovered but due to cost effect of the available drugs, most of the world's population is focusing on the natural remedies of medicinal plants. The current research study has explored the anti-plasmodial potential of Allium sativum against P. vivax. The methanolic extract of Allium sativum inhibited the P. vivax activity at the highest concentration of dose (80.57%). The assessment of anti-plasmodial effect of the methanolic Allium sativum extracts depends on the concentration of tested dose. This study supports the previously published study as discussed previously who reported the

anti-plasmodial potential of Allium sativum against different human protozoan's parasites(21). The phytochemicals analysis revealed Alliin, Allicin, Ajoenes, Vinyldithiins and Flavonoids. Allicin was the major compound that inhabited (59.75%) growth of P. vivax in vitro, which was comparable to the effect of Chloroquine and Nevaquine. The anti-plasmodial activity of Allium sativum is supported by the presence of several bioactive compounds which are identified in the current research study. Numerous studies have recommended that the polarity of the solute of interest should be taken into consideration when selecting the solvents to be utilized for extracting biomolecules from plants. The solute will dissolve correctly and with a high yield in a solvent with similar polarity to the solute(21). For most of the plant extraction, because of its polar character, which facilitates the extraction of various naturally occurring, biologically active chemicals present in plants, methanol is the suitable solvent(22). Since in animal's research studies the in vivo studies are more expensive, time-consuming, and subject to ethical debates as compared to *in-vitro* procedures. The *in-vivo* studies of testing the effects of medicinal plants are an important assay in research studies, which should be carried out in future. Moreover, further studies are required to isolate the pure biological active compounds of the mentioned classes in Allium sativum extract and to evaluate the in-vivo anti-plasmodial activities against P. vivax in future.

CONCLUSION

From the current study, it has been concluded that the methanolic extract of Allium sativum has strong anti-plasmodial activity in an in-vitro manner. An essential factor in evaluating the benefits of medicinal plants is their *in-vivo* potential. Therefore, further research studies are required to assess the *in-vivo* anti-plasmodial activities of Allium sativum against P. vivax.

Conflict of interest:
Authors declare no conflict of interest
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REFERENCES

1. World Health Organization. Malaria Report . 2003. Available from: https://iris.who.int/handle/10665/67869
2. Warrell DA. Essential Malariology, 4Ed . CRC Press; 2017.
3. World Health Organization. Malarial Report . 2012. Available from: https://www.who.int/publications/i/item/9789241564533
4. Carnevale P, Mouchet J. Prospects for malaria control. Int J Parasitol. 1987;17(1):181–7.
5. Kilama W, Ntoumi F. Malaria: a research agenda for the eradication era. Lancet . 2009 Oct;374(9700):1480–2.
6. Batiha GE-S, Alkazmi LM, Nadwa EH, Rashwan EK, Beshbishy AM, Shaheen H, et al. Physostigmine: A Plant Alkaloid Isolated from Physostigma venenosum: A Review on Pharmacokinetics, Pharmacological and Toxicological Activities. J Drug Deliv Ther . 2020 Feb 15;10(1-s):187–90.
7. Batiha GE-S, Beshbishy AM, Tayebwa DS, Adeyemi OS, Yokoyama N, Igarashi I. Evaluation of the inhibitory effect of ivermectin on the growth of Babesia and Theileria parasites in vitro and in vivo. Trop Med Health . 2019 Dec 11;47(1):42.
8. Baba MS, Zin NM, Hassan ZAA, Latip J, Pethick F, Hunter IS, et al. In vivo antimalarial activity of the endophytic actinobacteria, Streptomyces SUK 10. J Microbiol . 2015 Dec 2;53(12):847–55.
9. Ayaz E, Alpsoy HC. [Garlic (Allium sativum) and traditional medicine]. Turkiye parazitolojii Derg . 2007;31(2):145–9.
10. Badal DS, Dwivedi AK, Kumar V, Singh S, Prakash A, Verma S, et al. Effect of organic manures and

inorganic fertilizers on growth, yield and its attributing traits in garlic (Allium sativum L.). J Pharmacogn Phytochem. 2019;8:587–590.
11. Barnes J, Anderson LA, Phillipson JD. Herbal Medicines. 2nd ed. London: Pharmaceutical Press; 2002.
12. Rahman K. Historical Perspective on Garlic and Cardiovascular Disease. J Nutr . 2001 Mar;131(3):977S-979S.
13. Senapati S., Dey S, Dwivedi S., Swarup D. Effect of garlic (Allium sativum L.) extract on tissue lead level in rats. J Ethnopharmacol . 2001 Aug;76(3):229–32.
14. Awan KA, Butt MS, Ul Haq I, Suleria HAR. Investigating the Antioxidant Potential of Garlic (Allium sativum) Extracts Through Different Extraction Modes. Curr Bioact Compd . 2019 Feb 6;15(1):45–50.
15. Singh V, Kumar R. Study of Phytochemical Analysis and Antioxidant Activity of Allium sativum of Bundelkhand Region. Int J Life-Sciences Sci Res . 2017 Nov;3(6):1451–8.
16. Marfurt J, Chalfein F, Prayoga P, Wabiser F, Kenangalem E, Piera KA, et al. Ex Vivo Drug Susceptibility of Ferroquine against Chloroquine-Resistant Isolates of Plasmodium falciparum and P. vivax. Antimicrob Agents Chemother . 2011 Sep;55(9):4461–4.
17. Ahmed E-HM, Nour BYM, Mohammed YG, Khalid H s. Antiplasmodial Activity of Some Medicinal Plants Used in Sudanese Folk-medicine. Environ Health Insights . 2010 Jan 4;4:EHI.S4108.
18. Mirzaalizadeh B, Sharif M, Daryani A, Ebrahimzadeh MA, Zargari M, Sarvi S, et al. Effects of Aloe vera and Eucalyptus methanolic extracts on experimental toxoplasmosis in vitro and in vivo. Exp Parasitol . 2018 Sep;192:6–11.
19. Kwansa-Bentum B, Agyeman K, Larbi-Akor J, Anyigba C, Appiah-Opong R. In Vitro Assessment of Antiplasmodial Activity and Cytotoxicity of Polyalthia longifolia Leaf Extracts on Plasmodium falciparum Strain NF54. Malar Res Treat . 2019 Jan 21;2019:1–9.
20. Iberl B, Winkler G, Müller B, Knobloch K. Quantitative Determination of Allicin and Alliin from Garlic by HPLC*. Planta Med . 1990 Jun 5;56(03):320–6.
21. Altemimi A, Lakhssassi N, Baharlouei A, Watson D, Lightfoot D. Phytochemicals: Extraction, Isolation, and Identification of Bioactive Compounds from Plant Extracts. Plants . 2017 Sep 22;6(4):42.
22. Truong D-H, Nguyen DH, Ta NTA, Bui AV, Do TH, Nguyen HC. Evaluation of the Use of Different Solvents for Phytochemical Constituents, Antioxidants, and In Vitro Anti-Inflammatory Activities of Severinia buxifolia. J Food Qual . 2019 Feb 3;2019:1–9.

Research Article

EVALUATION OF RISK FACTORS AND CLINICAL OUTCOMES OF ACUTE RESPIRATORY FAILURE FROM POST RENAL TRANSPLANT RECIPIENTS: A FIVE-YEAR DATA OF A SINGLE CENTER

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ABSTRACT

Acute Respiratory Failure (ARF) requiring Intensive Care Unit (ICU) admission is a common complication following renal transplant and is a diagnostic and therapeutic challenge. This study aimed to evaluate etiological factors and clinical outcomes of ARF following a renal transplant. This was a retrospective observational study. Data was recruited from last five –years' records of Renal Transplant Unit of Dow University of Health Sciences, Karachi, Pakistan. Patients who developed ARF after renal transplantation whether requiring hospitalization (both in ICU or in ward) were included and their severity, etiologic diagnosis, and clinical outcomes were evaluated. During past five years (June 2017 till June 2023) a total of 450 kidney allografts were done and 35 patients (7.8%) developed ARF. Out of which 15 patients were shifted to the ICU. Mortality of female patients was higher as compared to males (26.1% versus 20.4%). Hypertension was found to be the most common comorbidity whereas glomerulonephritis was the most common cause of End Stage Renal Disease (ESRD).

Acute rejection was observed in 20.89% (n = 94) of recipients. Bacterial pneumonia was the most common cause of ARF, one patient needed on mechanical ventilation whereas two patients were dialysis dependent survivors. ARF following renal transplant is associated with higher mortality and loss of graft function because of compromised immunity. Anti-bacterial prophylaxis and early intensive management appears to help in improving the outcome while integrating the graft function.

Key Words: Acute Respiratory Failure, Acute Respiratory Distress Syndrome, Intensive Care Unit, Renal transplant.

INTRODUCTION

Kidney transplant accounts for around two-third of total organ transplants in various hospitals across the globe. Practically, kidney transplantation has significantly improved life quality and survival of end-stage kidney patients relatively at lower cost than routine dialysis (1). Furthermore, advancement in drug management, immunosuppressive drugs and understanding of immune modulation have decreased rate of acute rejection episodes (2). In addition, these advances have brought dramatic betterment in long-term results. Beyond these facts, renal transplant recipients possess long-term historical background of chronic kidney damage and routine dialysis in addition to other serious comorbidities such as diabetes and cardiovascular disease related with immune deficiencies (3). This combination of health dilemmas consequently leads to several complications including lung diseases (4).

Renal transplant recipients are particularly at higher risk for acute respiratory failure (ARF) during anti-lymphocyte globulin therapy or graft failure for rejection. Renal transplant recipients that are

often recommended to ICU admissions due to ARF, suffer from high graft loss in addition to high probability of mortality. Nonetheless, ARF drastically influences short as well as long-term consequences including the requirement for intensive care unit (ICU) sometimes among Renal Transplant Recipients (RTR) with ARF (5).

The epidemiological aspects of ARF in renal transplant recipients are crucially affected by various regional attributes. Several studies reveal that almost one-half of renal transplant recipients account for ARF (6). Nevertheless, 22.5% of kidney patients die generally within 90 days after transplantation, but most of the survivors are left with obsolete grafts. All complications relevant to pulmonary manifestations after kidney transplantation approximately range between 3-17% (1, 4).

Certain research findings certify that within one month of renal post-transplant duration, cardiogenic pulmonary edema is diagnosed in almost half of the patients (7). On the contrary, pulmonary toxicity related to drugs and opportunistic fungal contamination is clinically present with symptoms and need hospitalization within six months of renal post-transplant duration (8). Fungal and bacterial infections are the leading causes of mortality in patients with ARF after renal transplantation (9, 10). Some studies suggest major factors of ARF in kidney transplant candidates and suggest certain recommendations to control mortality rate in various hospitals in addition to provision of sufficient care and adequate treatment (11-13). However, current data in terms of respiratory complications that are prevalent in renal transplant recipients of developing countries is scarce and need more research and analysis. Therefore, this study was designed to evaluate outcomes of post renal transplant recipients in terms of management, survival and deaths related to ARF.

METHODS

This cross-sectional study was conducted at Renal Transplant Unit of Dow University Hospital, Dow University of Health Sciences, Karachi, Pakistan. This study involved patients who developed ARF post renal transplant anytime within three months' period. However, patients who developed ARF after this duration, or blood borne infections leading to septicemia, rejection or any other post renal transplant complication were not included in this study. Five-year data was obtained from the hospital record of the patients who underwent renal transplant and developed ARF afterwards including both who shifted to Intensive Care Unit (ICU) or not during the period from 1st January 2017 to 30th December 2022. All adult recipients (≥ 18 years old) of kidney transplant were screened for ARF while they were staying after surgery and their follow-up visits during the specified period. Parameters used to diagnose ARF were respiratory rate ≥ 30 breaths per minute, severe dyspnea or oxygen saturation less than 92% or arterial pressure of oxygen less than 60mmHg at room temperature without any mechanical support. Fiberoptic bronchoscopy was done to visually examine the airways of lungs. Life sustaining treatments were given on the discretion of attending physician that included non-invasive or invasive mechanical ventilation, renal replacement therapy, or vasopressors alone or in combination depending on the physical state of the patients. Decision for non-invasive and endothelial mechanical ventilation was also based on the evaluation of attending physician. The decision for non-invasive or invasive mechanical ventilation, renal replacement therapy, vasopressors were also determined by the attending physicians. The study was approved by the local medical ethics committee of Dow University of Health Sciences (IRB-2952/DUHS/EXEMPTION/2023/142) and was carried out as per the principles outlined in the Declaration of Helsinki. Confidentiality of data was maintained throughout the course of study.

Statistical analysis

Statistical analysis was done using Statistical Package for Social Sciences (SPSS) version 21.0. Frequency (n) and percentage (%) of patients were measured and chi-square test ($\chi 2$) was applied to compare statistical difference of the categorical variables among post renal transplant patients who were hospital survivors and hospital non-survivors keeping the level of probability(p) 5% at 95% Confidence Interval (CI) and a significant p-value <0.05.

RESULTS

In this retrospective cross-sectional study, 450 kidney allografts were done in five years' period at Renal Transplant Unit of Dow University of Health Sciences. Out of 450 patients 274 (60.89) were males and 176 (39.1%) were females. A total of 35 patients (7.8%) developed ARF. Among patients who developed ARF 15 were shifted to ICU. The outcome of 450 renal transplant recipients' in terms of mortality and survival is mentioned in flow chart in figure 1.

The baseline characteristics, demographics and clinical features of the study population are summarised in Table 1. The mean age of the population is 67.8 ± 1.83 years. Of the 450 subjects, males were 60.89% (n = 274), the mortality of female subjects is 26.1% (n = 46 out of 176) as compared to males 20.43% (n = 56 out of 274).

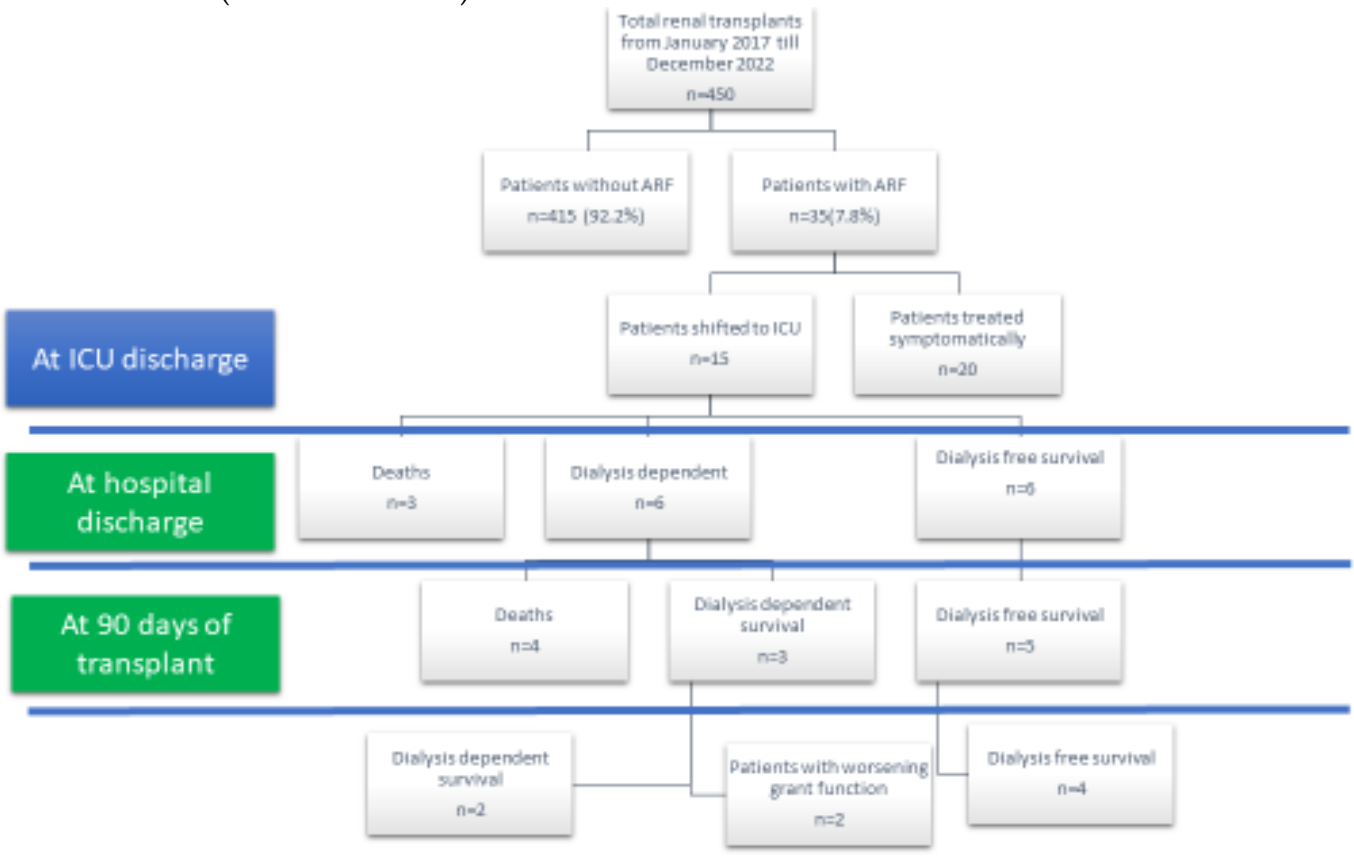

Figure 1. Summary of the patients underwent renal transplant and developed acute respiratory failure

Hypertension was found to be the most common comorbidity 82.67% (n = 372) whereas glomerulonephritis was the most common cause of ESRD 26.44% (n = 119) followed by nephroangiosclerosis 11.56% (n = 52). Acute rejection was observed in 20.89% (n = 94) of recipients whereas Cytomegalovirus (CMV) sero positivity was seen in 19.33% (n = 87) of subjects. Table 2

demonstrates characteristics of pulmonary involvement, severity and mechanical support for the patients admitted in ICU as per the cause of ARF.

Table 1. Summary of characteristics of patients underwent renal transplant and developed acute respiratory failure

S.no	Baseline characteristics		All patients N = 450 (%)	Hospital survivors N = 348 (%)	Hospital deaths N = 102 (%)
1.	Gender	Male	274 (60.89)	218 (62.64)	56 (54.9)
		Female	176 (39.11)	130 (37.36)	46 (45.1)
2.	Age (in years)	25-39	11 (2.22)	10 (2.87)	1 (1.0)
		40-49	23 (5.11)	21 (6.03)	2 (2.0)
		50-59	97 (21.56)	83 (23.85)	14 (13.7)
		60-69	177 (39.33)	123 (35.3)	54 (52.9)
		70 and above	142 (31.56)	111 (31.90)	31 (30.4)
3.	Comorbidities	Hypertension	372 (82.67)	316 (90.80)	56 (54.9)
		Heart failure	210 (46.67)	99 (28.45)	67 (65.9)
		Diabetes mellitus	124 (27.56)	67 (19.25)	57 (55.9)
4.	Causes leading to renal failure	Glomerulonephritis	119 (26.44)	93 (26.72)	24 (23.6)
		Nephroangiosclerosis	52 (11.56)	46 (13.22)	11 (10.8)
		Polycystic kidney disease	51 (11.33)	31 (8.91)	16 (15.7)
		Uropathy	29 (6.44)	27 (7.76)	6 (5.9)
		Diabetes mellitus	72 (16)	67 (19.25)	22 (21.7)
		Other undetermined causes	127 (28.22)	104 (29.89)	23 (22.6)
5.	Characteristics of transplant	First kidney allograft	294 (65.33)	219 (62.93)	75 (73.5)
		Kidney retransplanation	156 (34.67)	129 (37.07)	27 (26.5)
6.	Immuno suppressive agent	Cyclosporin	247 (54.89)	126 (36.21)	36 (35.3)
		Tacrolimus	162 (36)	57 (16.38)	38 (37.3)
		Mycophenolate mofetil	322 (71.56)	234 (67.24)	59 (57.9)
		Sirolimus	57 (12.67)	8 (2.30)	9 (8.8)
		Azathioprine	55 (12.22)	39 (11.21)	14 (13.7)
		Steroids	389 (86.44)	302 (86.78)	74 (72.6)
7.	Acute rejection		94 (20.89)	74 (21.26)	20 (19.6)
8.	Opportunistic infections	Cytomegalovirus disease, *n* (%)	87 (19.33)	66 (19.0)	23 (22.6)
		BK virus	43 (9.5)	27 (7.76)	16 (15.7)

DISCUSSION

The study presents the outcomes of post renal transplant patients in terms of survival and mortality. We have found that 22.67% of mortality post renal transplant out which 3.33% were secondary to ARF from a single centre.

These findings are in line with previously reported study where the rate was 2.9% (14). ARF is one of the serious problems in renal transplant recipients, mainly due to cardiogenic pulmonary edema and secondarily to lung injury in addition to bacterial pneumonia and COVID-19. It is because the study showed the data of last five years, out of which two years were affected by COVID-19 pandemic. Although, none of the study participant have ever suffered from COVID-19 during the study period and that could be considered as one of the main reasons of lower morbidity and mortality of patients who developed ARF. Nevertheless, early diagnosis of pneumonia in renal transplant recipients

reduces administration of excessive immunosuppressive drugs, but the use of glucocorticoids, antibiotics and antiviral agents is still made frequent (15-16).

Table 2. Characteristics of lung infiltration of patients admitted in Intensive care unit as per the cause of Acute Respiratory Failure

S. no.	Cause of ARF		Number of cases N (%)	Average duration since the onset of symptoms (in days)	Presence of ARDS at admission*	Lung infiltration**	Shock at admission***	Mechanical ventilation	Renal replacement therapy	Vasopressors administration
1.	Bacterial infection	Bacterial Pneumonia	6	2	5	4	4	3	3	3
		Extrapulmonary ARDS	2	1	2	1	2	1	1	2
2.	Cardiogenic pulmonary edema		2	1	3	4	1	2	1	1
3.	Opportunistic fungal infection	*Pneumocystis* pneumonia	2	7	2	3	-	1	1	1
		Invasive aspergillosis or Candidemia	1	8	1	1	-	-	-	-
		Viral pneumonia	1	5	1	1	-	-	-	-
4.	Drug-related pulmonary toxicity		1	7	1	1	-	-	-	-
	All patients		15	4	15	15	7	7	6	7

ARF= Acute Respiratory Failure, ARDS= Acute Respiratory Distress Syndrome. *diagosis of ARDS which depends on the ratio of partial pressure of arterial oxygen to fraction of inspired oxygen i.e. $PaO_2/FiO_2 \geq 200$, ** presence of lung infiltration in more than three quadrants on Chest X-ray.

Acute Respiratory Distress Syndrome (ARDS) accompanied by high level of creatinine in severe cases also leads to higher rates of deaths in renal transplant recipients (11, 17-19). Strategic measures of prevention, early diagnosis, appropriate treatment of respiratory disorders, sufficient nutrition to improve immune system are required to reduce incidence rate of ARDS (20, 21). Besides this, substantial use of invasive mechanical ventilation and adequate chemoprophylaxis is recommended to minimize the drastic consequences of ARF. This endorsement is highly crucial in decreasing death rates among pneumonia patients who have already gone through renal transplantation because of chronic kidney disease and low immunity (22-25).

The study was conducted from a single center for five years and a consecutive series of patients was recruited where the same treatment protocols were followed, thus this is considered as strength of

the study. However, retrospective nature of the study is considered as a limitation. With the evaluation of our data we agree with the current literature about the timely remedial measures to be taken to improve outcomes among post-renal transplant patients sustainable to develop such complications.

CONCLUSION

The study revealed that ARF accounts for 7.8% of total kidney transplantation, out of which 15 patients needed ICU management. A large number of graft recipients suffered to death or become dialysis dependent. In short, we can conclude that the outcome of post kidney transplant recipients who developed ARF depends on the underlying cause, comorbidity and the time taken to seek medical advice. The study suggests the addition of antibacterial and antifungal prophylactic drugs to reduce to incidences of ARF which would eventually help in better outcome.

Conflict of interest:
Authors declare no conflict of interest
Funding source:
The study did not receive any external funding
Ethical Approval:
The study was approved by the local medical ethics committee of Dow University of Health Sciences (IRB-2952/DUHS/EXEMPTION/2023/142) and was carried out as per the principles outlined in the Declaration of Helsinki. Confidentiality of data was maintained throughout the course of study.

REFERENCES

1. Canet et al.: Acute respiratory failure in kidney transplant recipients: a multicenter study. Critical Care 2011 15:R91.
2. Scala R, Heunks LJERR. Highlights in acute respiratory failure. Eur Respiratory Soc; 2018.
3. Hod T, Goldfarb-Rumyantzev ASJCt. Clinical issues in renal transplantation in the elderly. 2015;29(2):167-75.
4. Zhu L, Xu X, Ma K, Yang J, Guan H, Chen S, et al. Successful recovery of COVID-19 pneumonia in a renal transplant recipient with long-term immunosuppression. 2020;20(7):1859-63.
5. Butt Y, Kurdowska A, Allen TCJAoP, Medicine L. Acute lung injury: a clinical and molecular review. 2016;140(4):345-50.
6. Matthay MA, Zemans RL, Zimmerman GA, Arabi YM, Beitler JR, Mercat A, et al. Acute respiratory distress syndrome. 2019;5(1):1-22.
7. Chacko B, Peter JV, Tharyan P, John G, Jeyaseelan LJCDoSR. Pressure-controlled versus volume-controlled ventilation for acute respiratory failure due to acute lung injury (ALI) or acute respiratory distress syndrome (ARDS). 2015(1).
8. Huppert LA, Matthay MA, Ware LB, editors. Pathogenesis of acute respiratory distress syndrome. Seminars in respiratory and critical care medicine; 2019: Thieme Medical Publishers.
9. Banerjee D, Popoola J, Shah S, Ster IC, Quan V, Phanish MJKi. COVID-19 infection in kidney transplant recipients. 2020;97(6):1076-82.
10. Bello G, De Santis P, Antonelli MJAotm. Non-invasive ventilation in cardiogenic pulmonary edema. 2018;6(18).

11. Komiya K, Akaba T, Kozaki Y, Kadota J-i, Rubin BKJCC. A systematic review of diagnostic methods to differentiate acute lung injury/acute respiratory distress syndrome from cardiogenic pulmonary edema. 2017;21(1):1-10.
12. Moslehi MAJERoRM. Transbronchial Lung Cryobiopsy in children. 2022;16(3):333-9.
13. Russell JA, Gordon AC, Williams MD, Boyd JH, Walley KR, Kissoon N, editors. Vasopressor therapy in the intensive care unit. Seminars in Respiratory and Critical Care Medicine; 2021: Thieme Medical Publishers, Inc.
14. Katsounas A, Kamacharova I, Tyczynski B, Eggebrecht H, Erbel R, Canbay A, et al. The predictive performance of the SAPS II and SAPS 3 scoring systems: A retrospective analysis. 2016;33:180-5.
15. López-Izquierdo R, Brio-Ibañez Pd, Martín-Rodríguez F, Mohedano-Moriano A, Polonio-López B, Maestre-Miquel C, et al. Role of qSOFA and SOFA scoring systems for predicting in-hospital risk of deterioration in the emergency department. 2020;17(22):8367.
16. Darmon M, Canet E, Ostermann MJICM. Ten tips to manage renal transplant recipients. Springer; 2019. p. 380-3.
17. Mendonça DR, Aguiar CVN, Lins-Kusterer L, Correia LCL, Costa LMT, Menezes MSJAMP. Implementation of the Choosing Wisely Program in the General Surgery Residency. 2021;34(2):95-102.
18. Kerlin MP, Weissman GE, Wonneberger KA, Kent S, Madden V, Liu VX, et al. Validation of administrative definitions of invasive mechanical ventilation across 30 intensive care units. 2016;194(12):1548-52.
19. Walter JM, Corbridge TC, Singer BDJSmj. Invasive mechanical ventilation. 2018;111(12):746.
20. Canet, E., Osman, D., Lambert, J. et al. Acute respiratory failure in kidney transplant recipients: a multicenter study. Crit Care 15, R91 (2011). https://doi.org/10.1186/cc10091
21. Caillard S, Chavarot N, Francois H, Matignon M, Greze C, Kamar N, et al. Is COVID-19 infection more severe in kidney transplant recipients? 2021;21(3):1295-303.
22. Maggiore U, Abramowicz D, Crespo M, Mariat C, Mjoen G, Peruzzi L, et al. How should I manage immunosuppression in a kidney transplant patient with COVID-19? An ERA-EDTA DESCARTES expert opinion. Oxford University Press; 2020. p. 899-904.
23. Njau EW. Prevalence and determinants of dyslipidemias among renal transplant recipients attending nephrology clinic at Kenyatta national hospital: University of Nairobi; 2018.
24. Kaboutari-Zadeh L, Azizi A, Ghorbani A, Azizi AJIiMU. Designing and evaluating a mobile personal health record application for kidney transplant patients. 2022;30:100930.
25. Azoulay E, Mokart D, Lambert J, Lemiale V, Rabbat A, Kouatchet A, Vincent F, Gruson D, Bruneel F, Epinette-Branche G, Lafabrie A, Hamidfar-Roy R, Cracco C, Renard B, Tonnelier JM, Blot F, Chevret S, Schlemmer B. Diagnostic strategy for hematology and oncology patients with acute respiratory failure: randomized controlled trial. Am J Respir Crit Care Med. 2010;182:1038–1046. doi: 10.1164/rccm.201001-0018OC.

Research Article

PRESCRIBING TRENDS OF AMOXICILLIN, CEFTRIAXONE, AND MOXIFLOXACIN ACROSS DIFFERENT DISTRICTS OF KARACHI, PAKISTAN

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ABSTRACT

Antibiotic resistance is a major public health concern worldwide due to misuse and overuse of antibiotics. This study aimed to evaluate the dispensing trends of three frequently prescribed antibiotics including Amoxicillin, Ceftriaxone, and Moxifloxacin in various districts of Karachi. A cross-sectional study was conducted using a questionnaire distributed in pharmacies across different districts of Karachi, Pakistan. Data was analyzed to determine the dispensing trend of these three antibiotics. The results indicated that Amoxicillin was the most commonly prescribed antibiotic, followed by Ceftriaxone and then Moxifloxacin. District-wise analysis showed that Amoxicillin was the most commonly prescribed antibiotic in the south district. The frequent prescribing of these antibiotics has contributed to the antibiotic resistance. This study highlights the need for interventions to ensure rational prescribing practices so that antibiotic resistance can be prevented.

Key Words: Amoxicillin, Ceftriaxone, Moxifloxacin, Antibiotic resistance

INTRODUCTION

Dispensing drugs is a vital service provided by clinical pharmacists, which offers convenient access to prescription medications and over-the-counter drugs for a large number of patients (1). Dispensing medication involves evaluating prescriptions to ensure they are technically and legally sound, determining an individual's health needs, and providing pharmaceutical interventions such as counseling and documentation during the use of medicines (2). Pharmacies not only dispense drugs but also serve as information exchange centers where patients receive counseling and advice for their common health-related issues (3). In this process, pharmacists play a critical role in ensuring the safe and correct dispensing of drugs to patients (4).

Irrational drug use is one of the major causes of health-related problems (5). The World Health Organization (WHO) has reported that more than 50% of medicines are prescribed, dispensed, or sold incorrectly, and about half of the patients fail to use medicines appropriately, leading to overdose or underdose and serious health hazards (6). Among the many hazards associated with irrational drug use, antimicrobial resistance is the most significant threat to the general population

(6). Antibiotics are a class of drugs used to treat bacterial infections, and their overuse has led to the development of antibiotic resistance, making it difficult to treat a large number of infections (7).

The misuse and overuse of antibiotics is a growing problem worldwide, leading to increased antibiotic resistance. Self-medication with antibiotics has become a common practice in both developed and developing countries (8, 9), highlighting the need for health care workers to promote safe and rational use of drugs, particularly antibiotics (10). Health care workers can play a crucial role in this effort by educating patients about the proper use of antibiotics, encouraging adherence to treatment regimens, and discouraging self-medication with antibiotics. By promoting rational prescribing practices and responsible use of antibiotics, pharmacists can help combat antibiotic resistance and improve public health outcomes. It is essential for healthcare professionals to work together to promote effective antibiotic stewardship and prevent the emergence of antibiotic-resistant infections. Antibiotic resistance has been reported from all over the world. A report published in 2019 showed that 4.95 million people died due to antibacterial drug resistance. There is limited data available from Pakistan, thus this study was conducted to evaluate the dispensing trend of three antibiotics namely Amoxicillin, Ceftriaxone, and Moxifloxacin, at different pharmacies located in Karachi.

METHODS

This cross-sectional study was conducted over a period of six months, from January to June 2021, in various pharmacies located in Karachi, Pakistan.

Sampling and eligibility criteria:

Cluster sampling method was used where Karachi was selected as a cluster (representative of Pakistani population). Then Pharmacies were randomly selected, that met the eligibility criteria, including those located within hospital premises or in the community setting. Pharmacies from each district of Karachi (i.e. East, South, West, Malir, and Central) were included in the study. A minimum sample of 100 pharmacies was calculated using an online sample size calculator.

Research Instrument:

Ramay, Lambour (12) and Yu, Zhao (13) were referenced to develop the questionnaire for this study. The questionnaire was disseminated to various pharmacies in the area, where the pharmacy staff completed it and provided general information and data on the dispensing patterns of Amoxicillin, Ceftriaxone, and Moxifloxacin. An online version of the questionnaire was also prepared and sent via email to participating pharmacies, after informing the pharmacy administration of the study and receiving their consent. Participants were free to withdraw from the study at any point, and the confidentiality of their data and identity was ensured.

Statistical analysis

Data was analyzed using Statistical Package for Social Sciences (SPSS version 22.0). The responses were recorded and presented in the scores. Frequency distribution was presented in graphs.

RESULTS

A total of 108 pharmacies participated in the survey, distributed across different districts of Karachi. The majority of the pharmacies were located in the Central district (37.0%), while the smallest percentage of pharmacies (11.1%) were situated in the Malir district. The detailed distribution of pharmacies in each district is shown in Figure 1. The average number of prescriptions for Amoxicillin was the highest (n = 917), followed by Ceftriaxone (n = 712) and Moxifloxacin (n = 334). The mean duration of the establishment of the pharmacies was 7.7 years, ranging from 3 to 27 years.

The pharmacies received an average of 2961 antibiotic prescriptions per month. Table 1 provides information about the average number of patients who visited the pharmacy each month and the patients with a prescription of three antibiotics, namely Amoxicillin, Ceftriaxone, and Moxifloxacin. To evaluate the prescription patterns of the three antibiotics across different districts, a radar chart was constructed (Figure 2). It was observed that the mean prescriptions for Amoxicillin were the highest in every district, followed by Ceftriaxone and Moxifloxacin. Among the six districts, the mean prescriptions for Amoxicillin were highest for the South district (n = 1500), followed by East district (n = 1200) and Central district (n = 1000). The same trend was observed for Ceftriaxone and Moxifloxacin.

The trend of combined prescriptions of the three antibiotics in different districts of Karachi is presented in Figure 3. It was noted that the highest combined prescriptions were received in the Central district.

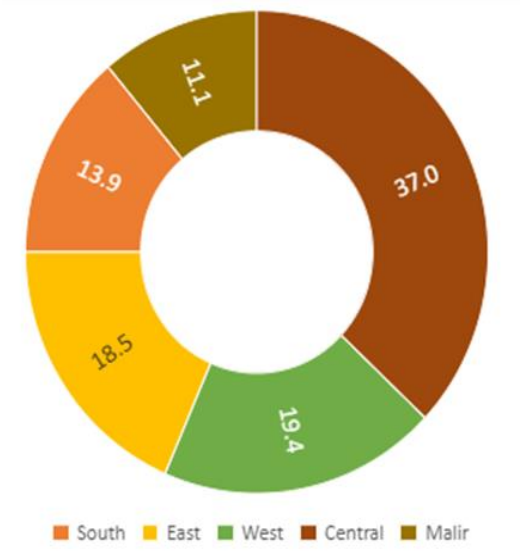

Figure 1: Allocation of pharmacies in districts

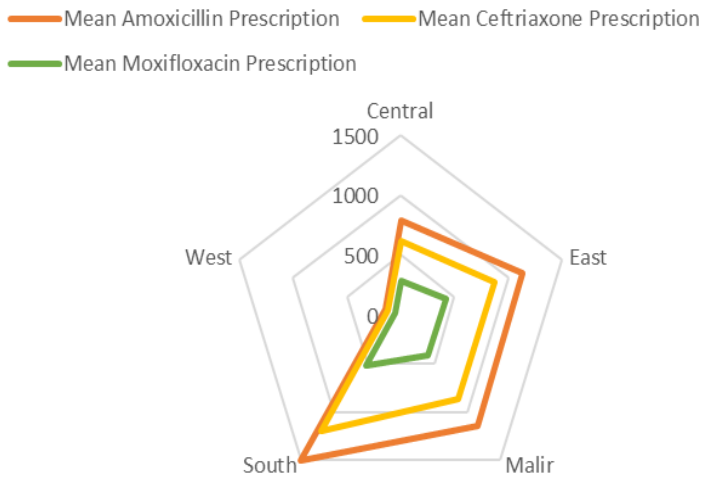

Figure 2: Prescriptions of Amoxicillin, Ceftriaxone, and Moxifloxacin according to districts

Table 1: Details of pharmacies

Question	Mean	Range
Duration of the establishment of the pharmacy (years)	7.7	3.0-7.0
Prescriptions of antibiotics each month	2961	300-10500
Patients with a prescription for Amoxicillin each month	917	90-3300
Patients with a prescription for Ceftriaxone each month	712	70-2500
Patients with a prescription for Moxifloxacin each month	334	25-1200

The sum of prescriptions of three antibiotics under study, i.e. Amoxicillin, Ceftriaxone and Moxifloxacin, is represented in Figure 4. The average number of prescriptions for Amoxicillin, Ceftriaxone and Moxifloxacin received per month in each district is indicated in Figure 5, Figure 6

and Figure 7 respectively. The highest average number of prescriptions received for Amoxicillin (1500 prescriptions per month), Ceftriaxone (1200 prescriptions per month) and Moxifloxacin (525 prescriptions per month) are in South District.

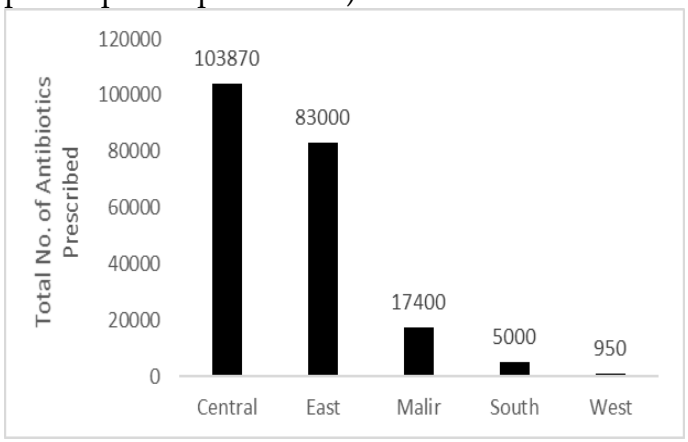

Figure 3: Trend of combined prescriptions of Amoxicillin, Ceftriaxone and Moxifloxacin in different districts of Karachi

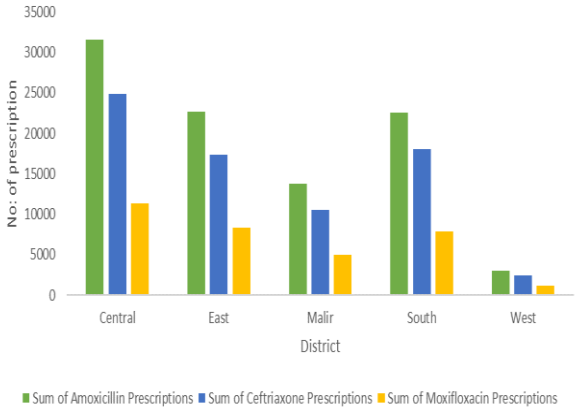

Figure 4: Trend of combined prescriptions of Amoxicillin, Ceftriaxone and Moxifloxacin

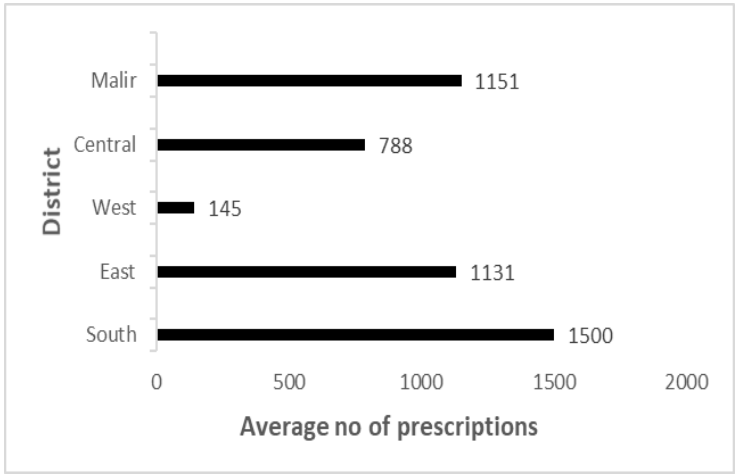

Figure 5: Average monthly prescriptions of amoxicillin in a single pharmacy of different districts of Karachi

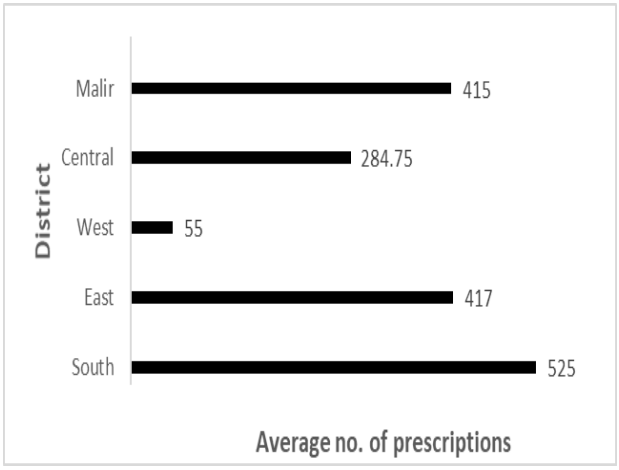

Figure 6: Average monthly prescriptions of Ceftriaxone in a single pharmacy of different districts of Karachi

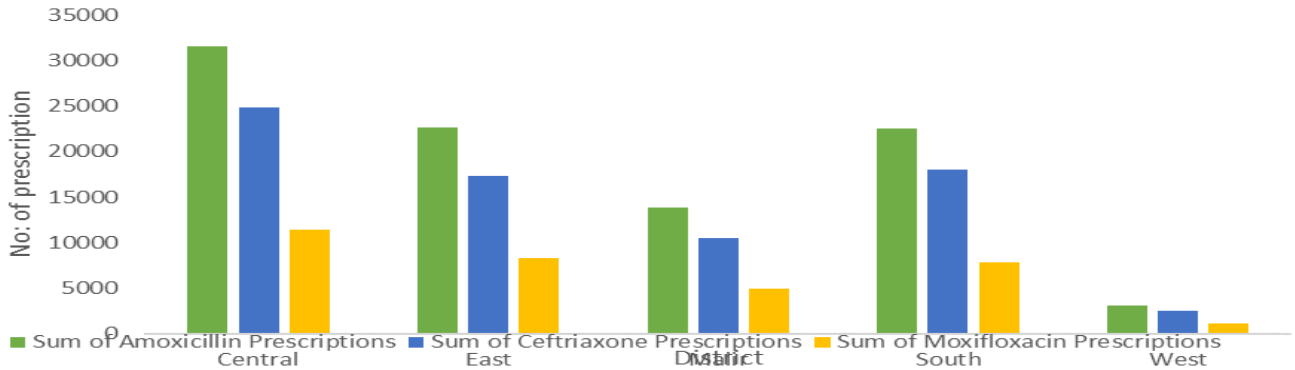

Figure 7: Average monthly prescriptions of Moxifloxacin in a single pharmacy of different districts of Karachi

DISCUSSION

Antibiotics are prescribed for infections, but their widespread use can promote the development of antibiotic resistance. Therefore, the rational use of antibiotics is crucial, which means prescribing the appropriate drug at the appropriate dose for the appropriate time period as and when needed (14). Literature from various research studies indicates that irrational and excessive use of antibiotics can result in several problems for the patient and society, including extra cost, frequent exposure to drug side effects, and the development of bacterial resistance against antibiotics (15). The rise in the population of resistant bacterial strains reduces the effectiveness of antibiotics, leading to increased morbidity and premature mortality (16). The current study focused on the consumption patterns of three commonly used antibiotics for respiratory tract infections, i.e., Amoxicillin, Ceftriaxone, and Moxifloxacin. The study was conducted in different community pharmacies located in all six districts of Karachi. The results of the study showed that the maximum number of prescriptions in all districts was for Amoxicillin, while the least number of prescriptions in all districts was for Moxifloxacin. Like other developing nations, Pakistan also has excessive and unnecessary use of antibiotics. One study conducted in Pakistan revealed that 13.45% of the total prescribed medicines consisted of antimicrobial drugs, while there were 45.19% of prescriptions that had at least one antibiotic prescribed to the patient (17). Results of different researchers suggest that antibiotics are the most widely used class of drugs to treat diseases, and their frequent use is responsible for the development of antibiotic resistance among the population (18, 19). The current study also showed large mean values for the prescriptions of antibiotics, particularly Amoxicillin, Ceftriaxone, and Moxifloxacin, in a month. These antibiotics belong to the class of Penicillin, Cephalosporins, and Fluoroquinolones, respectively. The study found that Penicillin was the highest-selling antibiotic followed by Cephalosporins and then Fluoroquinolones. This is contradictory to the results of the cross-sectional survey conducted in Bangalore, India which declared Cephalosporins as the highly prescribed antibiotic followed by Quinolones, anti-fungal, aminoglycosides, and then Penicillin (20). A similar style of ranking was observed in a study conducted in Bangladesh (21). This is probably the choice of the prescribing healthcare professionals. The study distributed questionnaires to pharmacies in different districts of Karachi, including South, East, West, Central, and Malir, to gather information on the number of prescriptions received for three antibiotics: Amoxicillin, Ceftriaxone, and Moxifloxacin. While, the Central district receives the most antibiotics prescriptions in general, the South district is leading in the sale of the three antibiotics under study. This might have influence of the catchment area and the choice of the doctor prescribing antibiotics. The effectiveness of antibiotics in curing infections can vary for various reasons. In a study, an equal percentage of people reported both success and failure in the use of antibiotics for treating their infections. Failure of the antibiotic treatment may occur due to several factors, including misdiagnosis or self-medication without proper diagnosis. If a patient has self-diagnosed their condition based on symptoms alone, without undergoing any confirmation test by a medical professional, then the prescribed antibiotic therapy may not be effective. It is important to consult with a healthcare provider and follow their advice regarding the use of antibiotics to ensure proper diagnosis and treatment (22).

It is essential to note that the use of antibiotics does not always produce a cure due to various reasons. For example, the disease may not disappear due to no infection, self-medication by the

patient, or misdiagnosis by the doctor. Therefore, it is crucial to perform confirmation tests to diagnose the infection accurately and prescribe appropriate antibiotic therapy. In this regard culture sensitivity is an essential test to be performed before prescribing any antibiotic. This test is also readily available in laboratories.

CONCLUSION

Antibiotic resistance has drastically increased due to the irrational use of antibiotics. The number of infections that were not considered critical and were easily treated with the use of antibiotics is becoming difficult to treat and ultimately resulting in increased cost of treatment. Strict actions needed to be taken by the health department to control the development of antibiotic resistance.

Conflict of interest:
Authors declare no conflict of interest
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Ethical Approval:
This study was approved by the Board of Advanced Studies and Research of the University of Karachi (ASRB/No. /02603/ Pharm.).

REFERENCES

1. Martins SF, Van Mil J, Da Costa FA. The organizational framework of community pharmacies in Europe. International journal of clinical pharmacy. 2015;37(5):896-905.
2. Pizetta B, Raggi LG, Rocha KSS, Cerqueira-Santos S, de Lyra-Jr DP, dos Santos Júnior GA. Does drug dispensing improve the health outcomes of patients attending community pharmacies? A systematic review. BMC health services research. 2021;21(1):1-12.
3. Rabbani F, Cheema F, Talati N, Siddiqui S, Syed S, Bashir S, et al. Behind the counter: pharmacies and dispensing patterns of pharmacy attendants in Karachi. JPMA: Journal of the Pakistan Medical Association. 2001;51(4):149.
4. Obreli-Neto PR, Pereira LRL, Guidoni CM, de Oliveira Baldoni A, Marusic S, de Lyra-Júnior DP, et al. Use of simulated patients to evaluate combined oral contraceptive dispensing practices of community pharmacists. PLoS One. 2013;8(12):e79875.
5. Bouvy JC, De Bruin ML, Koopmanschap MA. Epidemiology of adverse drug reactions in Europe: a review of recent observational studies. Drug safety. 2015;38(5):437-53.
6. World Health Organization. Promoting rational use of medicines: core components. World Health Organization, 2002.
7. World Health Organization. Antibiotic Resistance: World Health Organization; 2020 [cited 2022 22nd November].
8. Alhomoud F, Aljamea Z, Almahasnah R, Alkhalifah K, Basalelah L, Alhomoud FK. Self-medication and self-prescription with antibiotics in the Middle East—do they really happen? A systematic review of the prevalence, possible reasons, and outcomes. International Journal of Infectious Diseases. 2017;57:3-12.
9. Banerjee I, Sathian B, Gupta RK, Amarendra A, Roy B, Bakthavatchalam P, et al. Self-medication practice among preclinical university students in a medical school from the city of Pokhara, Nepal. Nepal J Epidemiol. 2016;6(2):574-81.

10. Blalock SJ, Roberts AW, Lauffenburger JC, Thompson T, O'Connor SK. The Effect of community pharmacy–based interventions on patient health outcomes: a systematic review. Medical care research and review. 2013;70(3):235-66.
11. Raosoft I. Sample size calculator [Internet]. Raosoft Retrieved December, 2020 from http://www.raosoft.com/samplesize.html.; 2014.
12. Ramay BM, Lambour P, Cerón A. Comparing antibiotic self-medication in two socio-economic groups in Guatemala City: a descriptive cross-sectional study. BMC Pharmacology and Toxicology. 2015;16(1):11.
13. Yu M, Zhao G, Stålsby Lundborg C, Zhu Y, Zhao Q, Xu B. Knowledge, attitudes, and practices of parents in rural China on the use of antibiotics in children: a cross-sectional study. BMC Infectious Diseases. 2014;14(1):112.
14. Organization WH. Medication safety in polypharmacy: technical report. World Health Organization, 2019.
15. Sunny TP, Jacob R, Krishnakumar K, Varghese S. Self-medication: Is a serious challenge to control antibiotic resistance? National Journal of Physiology, Pharmacy and Pharmacology. 2019;9(9):821-7.
16. Khalil I, Walker R, Porter CK, Muhib F, Chilengi R, Cravioto A, et al. Enterotoxigenic Escherichia coli (ETEC) vaccines: Priority activities to enable product development, licensure, and global access. Vaccine. 2021;39(31):4266-77.
17. Das N, Khan A, Badini Z, Baloch H, Parkash J. Prescribing practices of consultants at Karachi, Pakistan. JOURNAL-PAKISTAN MEDICAL ASSOCIATION. 2001;51(2):74-7.
18. Hameed A, Naveed S, Qamar F, Alam T, Abbas S, Sharif N. Irrational use of antibiotics. Different Age Groups of Karachi: a wakeup call for antibiotic resistance and future infections J Bioequiv Availab. 2016;8:242-5.
19. Nepal G, Bhatta S. Self-medication with antibiotics in WHO Southeast Asian Region: a systematic review. Cureus. 2018;10(4):1-17.
20. Jokandan SS, Jha DK. A Study Of Prescribing Pattern Of Antibiotics In A Tertiary Care Hospital-An Observational Study. Int J Pharm Sci Res. 2019;10(5):2285-89.
21. Biswas M, Roy DN, Tajmim A, Rajib SS, Hossain M, Farzana F, et al. Prescription antibiotics for outpatients in Bangladesh: a cross-sectional health survey conducted in three cities. Annals of clinical microbiology and antimicrobials. 2014;13(1):1-7.
22. Mustafa Z, Ghaffari M. Diagnostic methods, clinical guidelines, and antibiotic treatment for group A streptococcal pharyngitis: a narrative review. Frontiers in Cellular and Infection Microbiology. 2020;10:563627.

Research Article

RENAL VASCULAR DISPARITIES AMONG KIDNEY DONORS PRESENTED AT RENAL TRANSPLANT UNIT- A SINGLE CENTRE STUDY

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ABSTRACT
Renal vasculature has been reported to show anatomical variations, which may lead to surgical complications. The pattern of renal vascular variations in Pakistani population is not well reported. Thus, this study was designed to assess the renal vascularity among kidney donors and correlate with age, gender and site of vessels. A total of 223 healthy volunteers underwent evaluation for kidney donation at the Radiology Department, DOW University Hospital, Karachi, Pakistan from January 2020 to July 2022 were included. The assessment of renal vasculature was done on computed (CT) angiogram. Renal vascular variations were found in 112 (50.2%), 59.8% were seen in males and 40.2% in females. On right side 50% vascular anomalies were found followed by left side with 27% and 22% on both sides. The arterial variants included accessory renal artery seen in 76 (67.8%) individuals, out of which 13.2% had in upper polar, 26.3% in hilum, 36.8% in lower polar, while 23.7% of early branching was observed. Ten retro-aortic, fourteen accessory renal veins and six bifurcation renal veins, along with six early branching renal veins, were present. Patient who received donor nephrectomy, the outcomes of the operation were completely consistent with the results of the CTA. According to this study, Pakistani population have differences in their renal venous and arterial anatomy, which can significantly influence surgical procedures.

Key Words: Emergency obstetric hysterectomy, Depression, young women

INTRODUCTION

The renal vessels have been reported for exhibiting a wide variety of variances from cadaveric imaging studies. Due to the increasing frequency of kidney disease, transplant surgeons, nephrologists and radiologists are intensely interested in renal vascular variations. With the development of renal transplantation, variation in renal vascular anatomy has become more significant since it is critical in determining which kidney (left or right) to be transplanted(1). Variations in the arteries and/or veins of the kidneys are frequently observed in kidney donors (~ 48% and 53%). These differences include perihilar bifurcation (early branching), extra renal arteries, and unusual renal artery branching. Multiple renal veins, retro aortic, bifurcation, and early branching renal veins are examples of venous variant(2). End-stage renal disease (ESRD) is becoming more common across the globe, which presents a serious problem for the world's health care systems. The preferred course of treatment for ESRD is kidney transplantation, which is anticipated to dramatically improve a patient's quality of life. The most successful way for treating end-stage renal illness is kidney transplantation(3). The use of living donor kidney transplantation is rising as a result of a lack of cadaveric organs. Preoperative radiological examination of living donors is essential since the quality of the graft organ is what determines whether organ transplantation is successful. This necessitates precise imaging of the potential donor's renovascular systems, collecting system, and renal architecture. The renal vasculature can be quickly, safely, minimally invasively, and generally assessed before surgery using spiral computed tomography angiography (CTA). To prevent unintended consequences like venous and/or arterial injury during donor nephrectomy, it is especially crucial

to demonstrate renal artery variations accurately and in detail during the preoperative examination(4). To ensure the safety of the donor, Glomerular filtration rate (GFR) and albuminuria are two essential factors in determining the probability of long-term negative effects following donation. Both are used to identify the existence of renal disease. Urinary clearance of an ideal filtration marker is the "gold standard" for determining GFR, and albuminuria is typically determined from untimed "spot" urine samples using the albumin to creatinine ratio(5). Every living donor should undergo a thorough medical evaluation, which should include a thorough medical history, physical examination, blood and urine screening tests, an electrocardiogram, a chest X-ray, and imaging analysis of the kidney anatomy and its associated vasculature. The most prevalent application of CT angiogram, which has been shown to be a precise, safe, and economical procedure, is for the anatomical assessment of the renal donor. In some facilities, certain living kidney donor patients get MRI/MRA. Less frequently is ultrasound used during kidney examinations for living donors(6).

COMPUTED TOMOGRAPHY ANGIOGRAPHY (CTA):

A standard CTA procedure for evaluating Renal Healthy donor can undergo CTA imaging using a 4-phase CT image acquisition methodology. During first phase a non-contrast image acquisition is done followed by the arterial phase and nephron graphic phase, and finally excretory phase which is also known as pyelographic phase(7).

Acquiring Non-Contrast Images

This is the best phase to determine whether kidney stones or calcifications are present. However, given that the donor are healthy volunteers the arterial phase is considered to be sufficient for detecting kidney stones. In many centers this phase is not highly recommended. On CT scans, this could, however, lead to an increase in false-positive "stone" detection.

Arterial Phase CTA Image Acquisition

Automated bolus monitoring can be used in CTA for renal donors, much like it is in conventional CT angiography investigations to evaluate abdominal artery anatomy. An injection rate of 4 to 5 mL/s can be used to provide a nonionic contrast agent with a concentration of 300 or 370 mg iodine/mL. Depending on the iodine concentration, the maximum dose for the contrast should be 100 or 120 ml. The diaphragm dome and the distal part of the common iliac arteries, or the iliac crest, should be the best anatomic coverage for CTA. Another choice for getting the CTA is to slightly postpone the arterial phase image acquisition by 25–30 seconds. Some venous structures, such as the adrenal and gonadal veins, can be assessed using delayed arterial phase imaging.

Nephrographic Phase Image Acquisition

This phase is used to evaluate renal parenchymal status, where any renal mass can be excluded. This phase portrays renal venous architecture, which also includes smaller veins to the adrenal glands.

Excretory Phase Image Acquisition

This phase is taken between 4 to 8 minutes after contrast injection. During this phase whole collecting system is assessed for any pathology. In some centers only scout image is taken to avoid longer radiation exposure. Though, taking only scout image may pose a risk of missing any urothelial mass in a donor kidney.

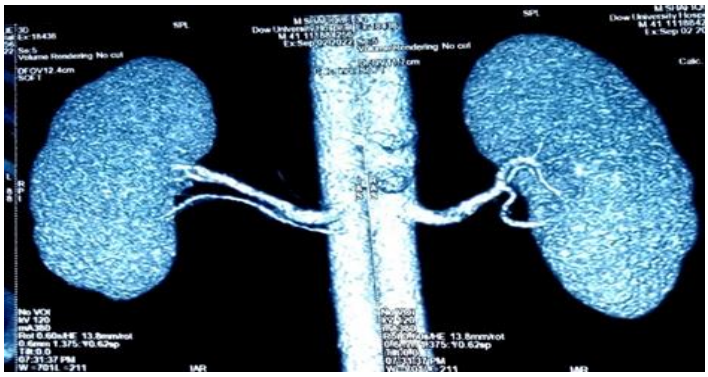
For patients with end stage renal disease kidney transplantation is the life-saving procedure. The detailed assessment of the donor kidney before transplantation is the essential component and greatly influences success of the transplantation. The assessment also includes renal vascular assessment of the donor in order to avoid any surgical complications. Currently CT angiography is the gold standard method.

There is always a chance of finding anatomical variations in humans including renal vasculature. This is particularly important in transplant procedures. There are a number of cadaveric reports where renal anomalies have been reported. However, there is limited literature available including living donors. Thus this study was designed to assess CT angiography of the living donor assessed for renal vasculature.

METHODS

The current study was carried out at the Renal Transplant Unit of the DOW University of Health Sciences' (OJHA Campus), Karachi, Pakistan. This was a retrospective cross-sectional study based on an institution and a review of old records from transplant unit. All kidney donors who had donor nephrectomy between 2020 and 2022 were the subject of the study. 24 patients' records from 247 kidney donor were excluded from this study because they had CT angiography done from other hospital.

a



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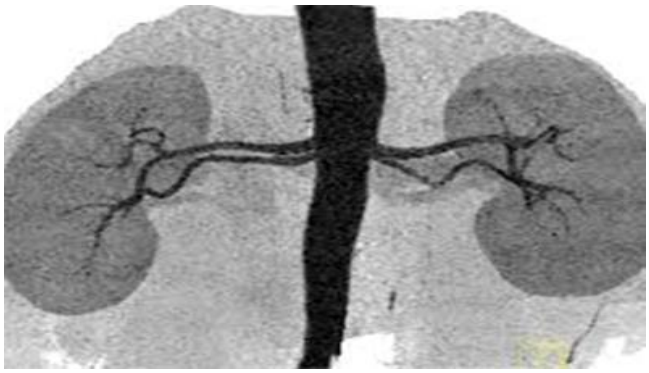

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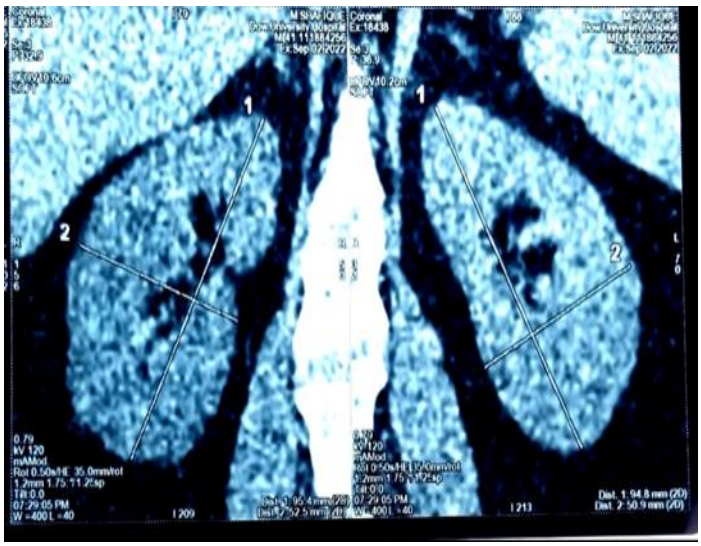

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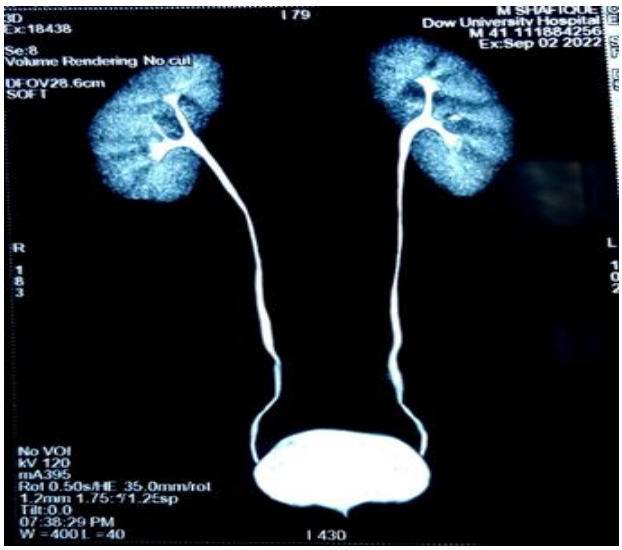

e

Figure 1. CT angiograms of different phases: a: Arterial Phase, b: Arteria Phase, two arteries on right side, c: Arterial phase, bilateral renal arteries d: Nephrographic phase e: Excretory phase

This study involved a total of 223 kidney donors. A standardized checklist was used to capture information about each kidney donor's age, sex, and description of the renal vascular anatomic reports made by radiologists (CT Angiography reading) and transplant surgeons in the centre. After a thorough examination of pertinent literature and comparable research, a data collection method was created to ensure the quality of the collected data.

In this study, we describe the pattern of vessels as follows: A major renal artery that has branched was referred to as an early branching renal artery. At the left side renal vein that runs posterior to the abdominal aorta between the aorta and empties into the inferior vena cava is known as the retro aortic renal vein. The left renal vein's division into its anterior and posterior limbs is known as the bifurcation of the renal vein.

Statistical analysis

After being coded, cleaned up, and entered into Epi-data version 4.4, all the collected data was exported to SPSS version 20 for analysis. Calculated descriptive statistics included frequencies and percentages. With regard to the gender and laterality, the information on the renal vascular structure was assessed. For categorical data, the chi-square test was used, and p-value< 0.05 was regarded as statistically significant.

RESULTS

Basic demographic features of kidney donors

A total of 223 individuals were included in this study, of which 103 (46.2%) were men and 120 (53.8%) were women kidney donors. The age of the donors ranged from 18 to 65 years, with a mean age of 34.36 years (±SD 10.02). The majority of the donors (~50.8%) were between the age of 20 and 30 years. However, it was significantly correlated with vasculature variation (p-value=0.630).

A total of 112 kidney donors showed vascular variation including 30.0% of male donors and 20.17% of female donors. Males substantially outnumbered than females in terms of the proportion of renal vascular alterations but it was not significantly correlate with gender (p-value= 0.38).

Pre-operative CT angiograms were performed of the donors to evaluate the renal vascular architecture. A statistically significant correlation between vascular variations and laterality was observed (p-value <0.001). A summary of vascular variations is presented in Table 1, which were more common at right side as compared to left side (25.1% versus 13.9% respectively) and variation on both sides was observed is 11.2% (Figure 2).

Table 2 showed number of vessels among gender. At right side double artery was more common among males than females (31.25% versus 13.39% respectively), while double vein were more common among females than males (14.3% versus 11.6% respectively). On left side double artery was more common among males than females (25.8% versus 15.2% respectively) while double vein was not common among females and only small proportion of males. Vasculature variation did not statistically correlate with laterality and number of vessels.

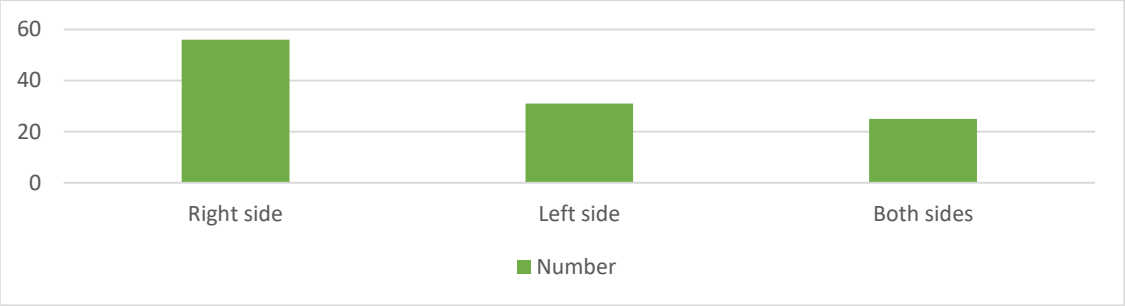

Figure 2. Demographic characteristics of kidney donors with vascular anatomy

Table 3 showed arterial and venous variations. The accessory renal artery was more commonly originated from lower pole (36.8%) while 23.7% early branching was observed in arterial variation. In venous variations, 16.7% showed accessory renal vein in males and 22.2% among females. Retro aortic veins (13.9%) and early branching (8.3%) are equally observed among males and females while bifurcation variation (16.7%) were identified only among females.

Table 1. Number of vessels in Kidney donors- males versus female donors

Number of vessels	Gender		Total (n=112)
	Male (n=67, 59.8%)	Female (n=45, 40.2%)	
Right Renal Artery			
Single	31(27.6)	28(25.0)	59(52.7)
Double	35(31.2)	15(13.4)	50(44.6)
Triple	1(0.9)	2(1.8)	3(2.7)
Right Renal Vein			
Single	53(47.3)	29(25.9)	82(73.2)
Double	13(11.6)	16(14.3)	29(25.9)
Triple	0(0.0)	1(0.9)	1(0.9)
Left Renal Artery			
Single	36(32.1)	26(23.2)	62(55.3)
Double	29(25.8)	17(15.2)	46(41.1)
Triple	3(2.7)	1(0.9)	4(3.6)
Left Renal Vein			
Single	66(58.9)	45(40.2)	111(99.1)
Double	1(0.9)	0(0.00)	1(0.9)
Triple	0(0.0)	0(0.0)	0(0.0)

Table 3: Presentation of vascular variation among kidney donors

Type of variation	Gender		Total
	Male	Female	
Arterial			
Upper Polar	6(7.9)	4(5.3)	10(13.2)
Hilar	8(10.5)	12(15.8)	20(26.3)
Lower pole	20(26.3)	8(10.5)	28(36.8)
Early branching	12(15.8)	6(7.9)	18(23.7)
Venous variation			
Accessory vein	6(16.7)	8(22.2)	14(38.9)
Retro-aortic vein	5(13.9)	5(13.9)	10(27.8)
Early branching	3(8.3)	3(8.3)	6(16.6)
Bifurcation	0(0)	6(16.7)	6(16.7)

DISCUSSION

The most effective form of treatment for ESRD is a kidney transplant. It is technically simpler to transplant kidneys with one renal artery than kidneys with several renal arteries. Furthermore, compared to kidney transplantation involving transplantation of kidneys with more than one renal artery, the postoperative rates

of complication and kidney loss are lower when transplanting kidneys with just one renal artery(11,12). For a successful graft nephrectomy, the surgeon must have precise preoperative knowledge of the donor's renal vasculature in order to lower the risk of vascular injury and decrease the time of ischemia. Renal CT angiogram is the most popular technique for assessing the donor's renal arteries. The kidney with a less complex vascular architecture is removed if both kidneys are healthy. Since the left kidney has a larger renal vein and is surgically simpler to remove, it is favoured for laparoscopic living donor nephrectomy(13–15). Right donor nephrectomy is preferred in several situations, such as complex left vascular anatomy or many auxiliary arteries. Because of this, CTA is crucial in selecting the best donor kidney based on the vasculature. According to earlier research, CTA can accurately identify donor vessels 95% to 100% of the time(12). All CTA results in our investigation were in agreement with the results of the operations on the harvested kidneys. Up to one-third of the general population can have accessory renal arteries, which are the most prevalent and clinically significant renal arterial variants. However, there is little chance that a kidney donor will have several renal arteries in both kidneys(16).

This study has shown a considerable number of healthy volunteers presenting with renal vascular variation. As reported previously there was predominance of males in having these variations (17). In this study 50.2% population had reported higher rate of renal vascular variation while 43.2% of renal variation reported in Iranian study conducted by Famurewa et al., in Nigerians reported rate was 50 %, while in Indians it was 59.5% (2,18). It can be inferred that the prevalence of renal vascular variations is extremely divergent in different populations and it is may be due to genetic differences across the populations. The frequency of anatomic alterations in the renal arteries vary among various ethnic and racial groups in the general population. Up to one-third of the normal population may have accessory renal arteries, which are the most prevalent and clinically significant renal arterial variation(19). However, it has been found that there is a low likelihood that a kidney donor will have more than one accessory renal artery in both kidneys(20). In the present study arterial and venous variations were more common on the right side, dissimilarly dominance of arterial variations in the left side were observed by Cinar et al(19). To the best of our knowledge, this study—in which CTA was utilized to assess renal arteries in almost 223 kidney transplantations—is the largest series in the literature. The fact that 67.9% of the donors had renal arteries visible on CTA is a significant finding in this dataset. This discovery, in our opinion, is extremely helpful in terms of giving the surgical team performing the donor nephrectomy a preliminary concept. It is well documented that the incidence of accessory renal arteries varies widely with population, ranging from 11.4 % in Kenyans to 59.5 % in Indians(21). Variation of renal artery were classified on the basis of their point of entry to the kidney, and the lower polar arteries were found to be the commonest (36.8%). This is due to the fact that kidneys ascend from the pelvic region during embryonic time; the most likely accessory renal arteries which fail to regress and persist will remain in the lower pole of the kidney(11, 22). Early branching of renal artery have immense importance during the transplantation, as failure of anastomosing them might lead to necrosis of a segment of the kidney and may require a surgeon to discard the graft(8). Moreover, Lower polar arteries may cause obstruction at the uretero-pelvic junction leading to hydronephrosis. During the renal transplantation, renal artery incision should be done 1.5–2 cm distal from the aortic origin to provide an easier haemorrhage control and to make anastomosis suitable. As a result, determining any possible early branching of the main renal artery is critical. The 23.7 % of early branching of the main renal artery reported in the present study. In accordance with previous studies, this study confirms the most frequent renal vein variation is accessory renal veins (38.9 %)(4). In angiographic and post-mortem studies, the prevalence of multiple renal veins was reported to be 11–28 %(23). Retro aortic left renal vein was found in eight donors, which in consistent with a previously reported study. Retro aortic left renal veins may have a high number of lumbar retroperitoneal tributaries, forming complex retro aortic systems, which can be easily injured during surgical dissection(23). This study excluded 24 kidney donors who had CT Angiogram from outside the DOW hospital. If all kidney

donor candidates had CT angiogram from other hospital, the chance of finding a more complex variant vasculature would increase.

CONCLUSION

This study concluded that Pakistani population have differences in their renal venous and arterial anatomy. The planning of surgical procedures can be significantly influenced by these variations and risk per-operative complications. To avoid diagnostic mistakes and to optimize surgical techniques to prevent undesired postsurgical morbidities, radiologists and surgeons need to be aware of all potential variants.

Conflict of interest:
Authors declare no conflict of interest
Funding source:
The study did not receive any external funding
Ethical Approval:
The data was retrospective analysis of hospital record, did not require ethical approval. At the time of transplant informed consent, patients and donors also consent for utilization of their information for research purpose.

REFERENCES

1. Gebremickael A, Afework M, Wondmagegn H, Bekele M. Renal vascular variations among kidney donors presented at the national kidney transplantation center, Addis Ababa, Ethiopia. Transl Res Anat . 2021 Nov;25:100145.
2. Famurewa O, Asaleye C, Ibitoye B, Ayoola O, Aderibigbe A, Badmus T. Variations of renal vascular anatomy in a Nigerian population: A computerized tomography study. Niger J Clin Pract. 2018;21(7):840.
3. Sarier M, Callioglu M, Yuksel Y, Duman E, Emek M, Usta SS. Evaluation of the Renal Arteries of 2,144 Living Kidney Donors Using Computed Tomography Angiography and Comparison with Intraoperative Findings. Urol Int . 2020;104(7–8):637–40.
4. Aghayev A, Gupta S, Dabiri BE, Steigner ML. Vascular imaging in renal donors. Cardiovasc Diagn Ther . 2019 Aug;9(S1):S116–30.
5. Inker LA, Huang N, Levey AS. Strategies for Assessing GFR and Albuminuria in the Living Kidney Donor Evaluation. Curr Transplant Reports. 2017 Mar 24;4(1):13–23.
6. Ikidag MA, Uysal E. Evaluation of Vascular Structures of Living Donor Kidneys by Multislice Computed Tomography Angiography before Transplant Surgery: Is Arterial Phase Sufficient for Determination of Both Arteries and Veins? J Belgian Soc Radiol . 2019 Apr 4;103(1).
7. Steinmetz JD, Bourne RRA, Briant PS, Flaxman SR, Taylor HRB, Jonas JB, et al. Causes of blindness and vision impairment in 2020 and trends over 30 years, and prevalence of avoidable blindness in relation to VISION 2020: the Right to Sight: an analysis for the Global Burden of Disease Study. Lancet Glob Heal . 2021 Feb;9(2):e144–60.
8. Hostiuc S, Rusu MC, Negoi I, Dorobanțu B, Grigoriu M. Anatomical variants of renal veins: A meta-analysis of prevalence. Sci Rep . 2019 Jul 25;9(1):10802.
9. Munnusamy K. Variations in Branching Pattern of Renal Artery in Kidney Donors Using CT Angiography. J Clin DIAGNOSTIC Res . 2016;
10. Black CK, Termanini KM, Aguirre O, Hawksworth JS, Sosin M. Solid organ transplantation in the 21st century. Ann Transl Med . 2018 Oct;6(20):409–409.
11. He B, Hamdorf J. Clinical importance of anatomical variations of renal vasculature during laparoscopic donor nephrectomy. OA Anat . 2013 Oct;1(3).
12. Muturi A, Kotecha V, Kanyi S. A retrospective study to assess the evaluation of living related kidney

donors and their outcomes following nephrectomy at Kenyatta National Hospital. BMC Nephrol . 2017 Dec 25;18(1):171.
13. Kachlík D, Varga I, Báča V, Musil V. Variant Anatomy and Its Terminology. Medicina (B Aires) . 2020 Dec 18;56(12):713.
14. Han WK, Na JC, Park SY. Low-dose CT angiography using ASiR-V for potential living renal donors: a prospective analysis of image quality and diagnostic accuracy. Eur Radiol . 2020 Feb;30(2):798–805.
15. Mohiuddin M, Mansoor A, Ali M, Hassan N. Analysis of renal artery morphometery in adults: A study conducted by using Multidetector computed Tomography Angiography. Pakistan J Med Sci . 2017 Aug 4;33(4).
16. Khush KK. Donor selection in the modern era. Ann Cardiothorac Surg . 2018 Jan;7(1):126–34.
17. Schold JD. The evolving role of regulatory reporting on patient and donor selection in organ transplantation. Curr Opin Organ Transplant . 2020 Apr;25(2):158–62.
18. Budhiraja V, Rastogi R, Jain V, Bankwar V. Anatomical variations of renal artery and its clinical correlations: A cadaveric study from central India. J Morphol Sci. 2013;30(4):228–33.
19. Çınar C, Türkvatan A. Prevalence of renal vascular variations: Evaluation with MDCT angiography. Diagn Interv Imaging . 2016 Sep;97(9):891–7.
20. Sungura R, Mathenge I, Onyambu C. The CT Angiographic Prevalence of Renal Accessory Arteries in Kenya. Int J Curr Microbiol Appl Sci. 2018 Jan 20;7(1):2745–54.
21. Manipal S. Renal artery variations: a cadaveric study with clinical relevance ijcrr. 2013;05(March):154–61.
22. Bachul PJ, Osuch C, Chang E, Bętkowska-Prokop A, Pasternak A, Szura M, et al. Crossing Anatomic Barriers—Transplantation of a Kidney with 5 Arteries, Duplication of the Pyelocalyceal System, and Double Ureter. Cell Transplant . 2017 Oct 21;26(10):1669–72.
23. Kawamoto S, Montgomery RA, Lawler LP, Horton KM, Fishman EK. Multi–Detector Row CT Evaluation of Living Renal Donors Prior to Laparoscopic Nephrectomy. RadioGraphics . 2004 Mar;24(2):453–66.

Research Article

DEPRESSION IN YOUNG WOMEN AFTER HYSTERECTOMY: EMERGENCY OBSTRETIC VERSUS ELECTIVE PROCEDURE – A COMPARATIVE CROSS-SECTIONAL STUDY

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ABSTRACT

Emergency obstetric hysterectomy (EOH) is done during cesarean section or after normal vaginal delivery, or any time during puerperal period. Puerperal period is usually associated with anxiety and depression in most cases, having emergency hysterectomy can potentially trigger it more. Therefore, this study was conducted to compare emergency versus elective hysterectomy to determine the pattern of depression between two groups. During a period of four years (from 1st march 2019 to 28th February 2023), a total of 6658 patients were admitted in obstetrics & gynecology department and 31 underwent emergency obstetric hysterectomies and consented to be part of this study. These females were aged between 18 to 49 years. For comparison 31 married control females were randomly selected and interviewed 3 months after undergoing elective hysterectomy due to gynecological conditions. There was no past family history for any psychiatric illness in both groups. The studied groups were clinically evaluated for major depressive episode according to the American Psychiatric Association diagnostic and statistical Manual of mental disorders, 4th edition text revised (DSM-IV TR) criteria. Beck depression inventory (BDI)18 to assess the severity of major depressive episodes. Out of 31 patients 16 cases were performed after caesarean section, four during laparotomy for ruptured uterus and 11 for uterine atony after normal vaginal delivery. There was significantly higher rate of depression among patients undergoing emergency hysterectomy as compared to those with elective procedure. The frequency of complications was also observed to be higher in emergency cases. Our study concluded that the frequency of complications and severe depression was remarkably higher in the obstetric emergency hysterectomy group as compared to the elective hysterectomy group.

Key Words: Emergency obstetric hysterectomy, Depression, young women

INTRODUCTION

Emergency obstetric hysterectomy (EOH) is the removal of uterus during cesarean section or after normal vaginal delivery any time during puerperium period. In emergency cases it is indicated when there is life-threatening situation such as severe hemorrhage (1). Women undergoing emergency hysterectomy have been reported to be at higher risk of mental health disorders (2). These disorders range from agitation, insomnia (3), non-specific anxiety(4), reduced psycho-sexual functioning(5,6), psycho-somatic disorders(7) to severe depression. European studies have considered depression as the major complication of emergency hysterectomy (8). It was also reported that younger women are at relatively higher risk of developing depressive disorders (9-12). As the younger women (in particular those under 40 years), consider uterus as a sexual organ and relate it to the child bearing capacity, thus post-operative depression is related to their parity (13,14). This has influence of social tabos and pressures from society. Furthermore, in cases of emergency hysterectomy women are not prepared for the loss, which those women undergoing elective procedure made the informed decision for a pre-diagnosis of indication of hysterectomy. Women with poor general health, lack of proper antenatal care and those from lower social-economical group are at higher risk of emergency hysterectomy. However, there is limited literature available studying post-operative depression in these

women. Thus this study was conducted to determine the frequency of depression following emergency obstetric hysterectomy and comparing with same age group women undergoing elective hysterectomy.

METHODS

This was a prospective comparative cross-sectional study conducted during a period of four years (from 1st March 2019 to 28th February 2023) at private sector Hospital in Hyderabad, Pakistan. A total of 6658 patients were admitted in Obstetrics & Gynecology Department during the study duration, out of which 32 underwent emergency obstetric hysterectomies and included in this study.

For comparison 31 married women undergoing elective hystrectomy during the same period were recruited. After 3 months of the procedure they were interviewed for evaluation of major depressive episode (MDE). The data of indications and complications was also collected in both groups. These all patients had no personal or family history of any mental health issues in both groups.

The clinical evaluation for MDE was done following the American Psychiatric Association diagnostic and statistical Manual of mental disorders, 4th edition text revised (DSM-IV TR) criteria. Beck depression inventory (BDI)18 was used to assess the severity of MDE. The criteria were comprised of a total of twenty-one questions and the responses were valued from 0 to 3. The interpretation was made according to the cumulative score; where ≤9 was labelled as not depressed, from 10 to 18 was mildly depressed, from 19 to 29 was moderately depressed and ≥30 was severely depressed.

Data were analyzed by using statistical package for social sciences software (SPSS) version 20. Data was presented as frequency and percentages. For comparison Chi-squared test was used and a p-value <0.05 was considered as significant

RESULTS

A total number 6658 women delivered during the study period, including 2338 cesarean sections. Emergency hysterectomies were performed in 31 (0.38%) women, making it 1 in 214 deliveries. A summary is presented in Table 1. There were 16 hysterectomies following a caesarean section, four after ruptured uterus and 11 after normal vaginal delivery due to uterine atony. Morbidly adherent placenta was reported in 11 patients (35.48%), placenta previa in 5(16.1%) patients, 4(12.9%) had ruptured uterus, 7 (22.5%) uterine atony, while 4(12.9%) patients had placental abruption (Table 2). The elective hystrectomies were performed in most cases due to abndomral uterine bleeding and fibroids (Table 2). Major depressive episodes were reported to be positive in 24(77.4%) patients of emergency obstetric hysterectomy. Of which 6(19.3%) has mild,15(48.3%) moderate and 3(9.6%) had severe episodes according to BDI score. As compared to elective hysterectomy 18 (58%) had MDE, of which 10(32.2%) were mild ,7(22.5%) moderate while 1(3.2%) patient experienced severe episodes (Figure 1). The rate of complications was also reported to be higher in emergency groups including one death (Table 3).

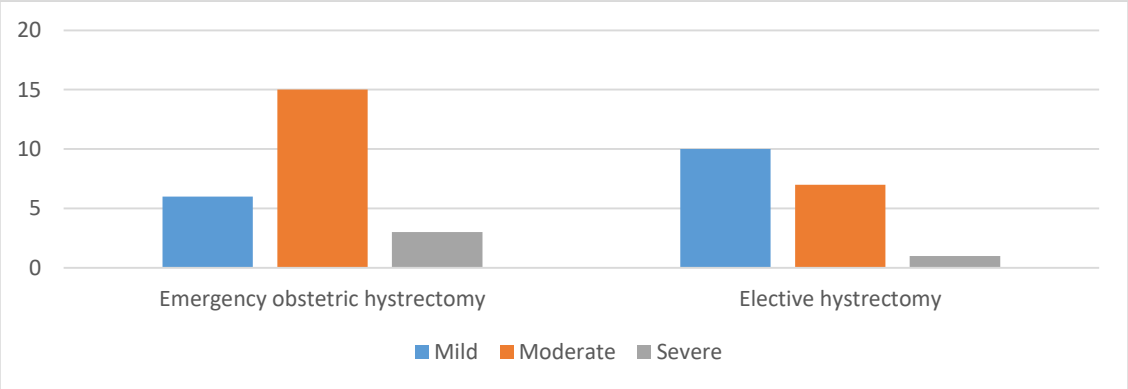

Figure 1. Severity of depression after Hystrectomy: emergency versus elective procedures

Table 1. Demographic characteristics of study population- Emergency Obstetric Hysterectomy versus Elective Hysterectomy

Variables	Emergency Obstetric Hysterectomy (A)	Elective Hysterectomy (B)
• Age groups		
15-25	13(41.9%)	1
26-35	16(51.6%)	04(16.1%)
36-45 46-65	2(6.5%) 00	(32.3%) 16(51.6%)
Total	31(100.0%)	31(100.0%)
• Gestational age		
<34 weeks	19(61.2%)	00
>36weeks	12(38.8%)	00
Total	31(100.0%)	31(100.0%)
• Educational status		
Illiterate	0(0%)	02(6.5%)
Primary	12(38.7%)	08(25.8%)
Metric	15(48.4%)	14(45.2%)
Graduate	4(13.0%)	07(22.6%)
Total	31(100.0%)	31(100.0%)
• Socioeconomic status		
Low	6(19.4%)	0(0%)
Middle	23(74.2%)	28(90.3%)
High	2(6.5%)	03(9.7%)
Total	31(100.0%)	31(100.0%)
• Hemoglobin	6.57±1.20	8.10±0.94
Pre-operative blood transfusions 1 2 >2	 12(38.7%) 13(31.9%) 6(19.4%)	 23(74.2%) 8(25.8%) 0(0%)
Post-operative blood transfusions 1 2 >2	 15(48.8%) 12(38.7%) 4(12.9%)	 27(87.1%) 4(12.9%) 00

DISCUSSION

Emergency Obstetric hysterectomy is performed in cases of life threatening situation during labor or puerperal period to save mother's life. In women presenting with placental abnormalities including placenta Previa pose a higher risk of emergency hysterectomy even after caesarean sections (15). The elective hysterectomies are on the other hand performed when there are clear indications before the procedure is planned, where in most cases women are willing to get it done due to bothersome symptoms.

Table 2. Indications of Hysterectomy in two groups- Emergency Obstetric Hysterectomy versus Elective Hysterectomy

Emergency Hysterectomy			
S.N0	**Indications**	**frequency**	**percentages**
1	Morbidly adherent placenta	11	35.48%
2	Uterine atony	7	22.5%
3	Placenta Previa without adherence	5	16.1%
4	Couvelaire uterus/Placental abruption	4	12.9%
5	Ruptured uterus	4	12.9%
Elective hysterectomy			
S.N0	**Indications**	**frequency**	**percentages**
1	Abnormal uterine Bleeding	12	38.7%
2	Fibroid uterus	5	16.1%
3	Uterine perforation due to induced abortion & sepsis	2	6.4%
4	Carcinoma of cervix	2	6.4%
5	Carcinoma of uterus	4	12.9%
6	Carcinoma of ovary	3	9.6%
7	Choriocarcinoma	2	6.4%
8	Post menopausal bleeding	1	3.2%

Table 3: Complications of emergency obstetric hysterectomy and elective hysterectomy

Intraoperative	**Emergency obstetric hysterectomy**	**Elective hysterectomy**
Bladder injury	13(40.6%)	9(29%)
Bowel injury	3(9.6%)	7(22.5%)
Bleeding	17(54%)	5(16.1%)
Postoperative		
Re-exploration laparotomy	3(9.6%)	2(6.4%)
Urinary tract infection	15(48.3%)	16(51.6%)
Chest infection	13(41.9%)	7(22.5%)
Wound infection	6(19.3%)	4(12.9%)
Acute renal failure	5(16.1%)	1(3.2%)
Disseminated intravascular coagulation	5(16.1%)	0(00%)
Vesico-vaginal fistula	3(9.6%)	2(6.4%)
Maternal death	1(3.2%)	0(00%)

While the women who undergoing the removal in emergency cases, they find it difficult to cope with the loss of their uterus and relating it's to their motherhood and sexuality and this makes their decision to consent for surgery challenging. In certain situations, women relate it to the loss of feminity (16). These all factors contribute to the development of depressive disorders of a certain degree. In our study results were suggestive of high tendency of MDE in women underwent emergency obstetric hysterectomy as compared to

those undergoing elective hysterectomy. It is in line with previously reported studies where younger women were 4 times more likely to suffer from depression than women whose uterus was saved (17). There is however a variation in the rate of depression in different studies which is likely to be due to the reporting rate, understanding by the patients and statistical power of the analysis. There are also social factors which might influence reporting of the depression. The availability of social support might also play a role in certain situations. However, in all the reported cases the development of depression was post-operative and obviously pointing a relation with hysterectomy (18). As reported depression is the most common psychiatric risk after hysterectomy (19), however in some women depression developed later as during initial period they were not depressed (20). In our study MDE were reported in 77% of patients in emergency obstetric hysterectomy, including 19.3% mild, 48.3% moderate and 9.6% severe episodes according to BDI score. As compared to elective hysterectomy 58% had MDE, of which 32.2% mild, 22.5%, 3.2% moderate while 3.2% patients experienced severe episodes respectively. A previously reported study including 300 patients between 25 to 50 underwent hysterectomy were studied, 37% of women reported to have depression (21). There are also reports of having short term and long term mental health issues (22). The removal of uterus is perceived socially as the loss of ability to produce children, and women take it as loss of feminity and attractiveness. Thus contributing a great deal to the development of anxiety and results in depression. The loss of ability to produce children is reported to be seen in women who are multiparous so it's not limited to having less children (23). In majority of cases these women are less than 40 years of age, thus the risk of depression is negatively proportional to the advancing age (17) . In addition, the risk of psycho-social factors, poverty, poor general health conditions contributing to the cause for hysterectomy also contribute to the development of mental health issues (24,25, 26). This study has strength of being a large scale study to look at the rate of emergency hysterectomies in a hospital setting where a consecutive series of patients were included. Thus the rate of the reported emergency hysterectomies was very low. The interviews taken might have some influence of the interviewer assisted mode of the data collection. This study has strength of comparing it with non-emergency hysterectomy patients so that the findings can be validated. Though the coping strategies and the long term follow-up were not included in this study, thus considered as the limitations of the study.

CONCLUSION

The rate of complications and severe depression was remarkably higher in the obstetric emergency hysterectomy group. Patients after emergency hysterectomy must be followed-up for symptoms of depression so that early management can be offered.

Conflict of interest:
Authors declare no conflict of interest
Funding source:
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Ethical Approval:
This study was approved by Local Ethics Committee.

REFERENCES

1.Say L, Souza JP, Pattinson RC. Maternal near miss – towards a standard tool for monitoring quality of maternal health care. Best Pract Res Clin Obstet Gynaecol 2009 Jun;23(3):287-296.
2. Gath D, Cooper P, Day A. Hysterectomy and psychiatric disorder: I. Levels of psychiatric morbidity before and after hysterectomy. Br.J.Psychiatry 1982; 140:335-42.
3. Lindemann E. Observations on psychiatric sequelae to surgical operations in women. Am.J.Psychiatry 1941; 98:132-9.

4. Drellich MG, Sutherland AM. The psychological impact of cancer and cancer surgery: Adoption to hysterectomy. The Ninth Annual Cancer Symposium of the James Ewing Society; 1956.
5. Ellison RM. Psychiatric complications following sterilization of women. Med.J.Aust. 1964; 2:625-8.
6. Dennerstein L, Wood C, Burrows GD. Sexual response following hysterectomy and oophorecomy. Obstet.Gynecol. 1977; 49(1):92-6.
7. Zervos SK, Papaloucas AC. Psychosomatic disturbances following hysterectomy performed at a premenopausal age. Int.Surg. 1972; 57(10):802-4.
8. Patterson RM, Craig JB. Misconceptions concerning the psychological effects of hysterectomy. Am.J.Obstet.Gynecol. 1963; 85:104-11.
9. Bragg RL. Risk of admission to mental hospital following hysterectomy or cholecystectomy. Am.J.Public Health Nations Health 1965; 55:1403-10.
10. Wolf SR. Emotional reactions to hysterectomy. Postgrad. Med. 1970; 47(5):165-9.
11. Ackner B. Emotional aspects of hysterectomy. A follow-up study of fifty patients under the age of 40. Fortschr. Psychosom. Med. 1960; 1:248-52.
12. Drellich MG, Bieber I. The psychologic importance of the uterus and its functions: Some psychoanalytic implications of hysterectomy. J. Nerv. Ment. Dis. 1958; 126(4):322-36.
13. Barker MG. Psychiatric illness after hysterectomy. BMJ 1968; 2:91-5.
14.Alipour A, Pour Y. Effect of cognitive behavioral therapy in hastening recovery of women after hysterectomy surgery. *J Behav Sci.* 2010;4(2):91–5.
15. Mazhar S, Haider F, MALIKA .Obstetric Hysterectomy and its Associated Maternal Morbidity and Mortality. P J M H S Vol. 10, NO. 4, OCT – DEC 2016.
16. Tsoh JM, Leung HC, Ungvari GS, Lee DT: Brief acute psychosis following hysterectomy in ethnopsychiatric context. Singapore Med J 2000, 41(7):359-62.
17.Richards DH. Depression after hysterectomy. Lancet 1973; 2(7826): 430-3.
18.Carlson KJ, Miller BA, Fowler FJ,Jr. The Maine Women's Health Study: I. Outcomes of hysterrectomy. Obstet.Gynecol. 1994; 83(4):556-65.
19. Naughton MJ, McBee WL. Health-related quality of life after hysterectomy. Clin.Obstet.Gynecol. 1997; 40(4):947-57.
20. Kjerulff KH, Langenberg PW, Rhodes JC, et al. Effectiveness of hysterectomy. Obstet.Gynecol. 2000; 95(3):319-26.
21.DeCherney AH, Bachmann G, Isaacson K, et al. Postoperative fatigue negatively impacts the daily lives of patients recovering from hysterectomy. Obstet.Gynecol. 2002; 99(1):51-7. 26.
22.Flory N, Bissonnette F, Kaltreider NB, Wallace A, Horowitz MJ. A field study of the stress response syndrome. Young women after hysterectomy. JAMA 1979; 242(14):1499- 503.
23.Binik YM. Psychosocial effects of hysterectomy: Literature review. J.Psychosom.Res. 2005; 59(3):117-29.
24.Cooper R, Mishra G, Hardy R, et al. Hysterectomy and subsequent psychological health: Findings from a British birth cohort study. J.affect. Disord. 2009; 115(1-2):122-30.
25. Leppert PC, Legro RS, Kjerulff KH. Hysterectomy and loss of fertility: Implications for women's mental health. J.Psychosom.Res. 2007; 63(3):269-74.
26. Ewalds Kvist SB, Hirvonen T, Kvist M, et al. Depression, anxiety, hostility and hysterectomy. J.Psychosom.Obstet.Gynaecol. 2005; 26(3):193-204.

Research Article

EFFECT OF ANTI-EPILEPTIC DRUGS ON SERUM LIPIDS IN EPILEPTIC PATIENTS- A CASE-CONTROL STUDY

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ABSTRACT

Epilepsy is a chronic illness, thus antiepileptic drugs are often used extensively. However, this treatment may be linked to metabolic abnormalities in different body systems, including the endocrine system, connective tissues, and liver. Moreover, prolonged use of antiepileptic drugs may lead to adverse effects on serum lipid levels. This study was conducted to explore alterations in serum lipids after the administration of antiepileptic drugs in epileptic patients and compared with healthy volunteers. A total of 200 participants were selected; including 100 epileptic patients and 100 age, gender and locality matched controls having negative personal or family history of epilepsy. All the participants signed written informed consent and were interviewed through a standard questionnaire. Blood samples were collected from all participants, for the analysis of serum lipids. The accurate rapid test used to analyze samples of both groups. Significantly increased concentration of total lipids, total cholesterol, triglyceride and VLDL-C were found in epileptic patients as compared to controls and also in male epileptic patients, whereas, reverse was true for HDL-C. Significant variations were found for total cholesterol, HDL-C, LDL, triglycerides and VLDL-C in epileptic patients with age group 36 to 46 years, while, the HDL-C was significantly decreased in age group 15 to 35 years.

Key Words: antiepileptic drugs, lipid profile, total cholesterol, triglycerides

INTRODUCTION

Epilepsy refers to a disorder of the brain characterized by the periodic and unpredictable occurrence of seizures and the most common neurologic conditions and a significant reason for incapacity and mortality (1, 2). Epilepsy, an illness of the sensory system which can be seen in all age groups. It is reported as the most common non-transmittable disease of the world (3). Epilepsy imposes considerable economic burden on the medical services around the globe. As 70-80% of patients take regular medication after developing epilepsy with the hope to have their seizures controlled with the ideal antiepileptic treatment. Population based investigations suggest the rate of epilepsy in children is around 3.6 to 4.2 per 1000 for children in developing countries and the rate is roughly double in non-industrial countries (4). Antiepileptic drugs are utilized for counteraction of the recurrence of seizures. Most commonly used drugs for epilepsy include carbamazepine (CBZ), phenytoin (DPH), phenobarbitone (PB), sodium valproate, lamotrigine (LTG), Topiramate (TPM), clobazam (CLB), oxcarbazepine (OXC) and levetericitam (LEV) (5). Prolonged use of antiepileptic treatment could have some unwanted effects on the lipid profile of the patients (6). Increase serum concentrations of lipids are related to an increased risk of cardiovascular diseases, may result in ischemic heart disease and

stroke (7). The number of patients taking epileptic drugs in Pakistan is also at rise, however there is limited data available to explore pattern of lipid profile in these patients. Thus, this study was designed to investigate the impact of antiepileptic drugs on serum lipid levels.

METHODS

This was a case-control study, carried out at the Institute of Biochemistry, University of Sindh, Jamshoro, Pakistan. The study population was selected from the Dadu district in Sindh. The sample consisted of 50 epileptic patients (cases) and 50 controls who were matched for age, sex, and locality having negative personal or family history of epilepsy. Prior to the commencement of the study, ethical approval was obtained from the Institutional Ethical Committee, and informed written consent was obtained from all participants in their native language. A standard questionnaire was designed for this study, which included questions about the participants' socio-demographic characteristics, lifestyle, diet, the impact of the sun exposure on them, and the use of antiepileptic drugs and its duration. Fasting blood samples were collected from all participants for the analysis of lipid profile parameters such as Total Lipids (TL), Total Cholesterol (TC), High Density Lipoprotein Cholesterol (HDL-C), Low Density Lipoprotein Cholesterol (LDL-C), Triglycerides (TG), and very Low-Density Lipoprotein Cholesterol (VLDL-C). Approximately 3ml of blood was drawn from each participants and collected in sterilized sample vials with a screw cap. The serum was separated and stored at -20°C for further analysis. The patient and control samples were analyzed using an accurate and rapid test at the Diagnostic and Research laboratory, Liaquat University of Medical and Health Sciences, Dadu Branch, using same standard protocol.

Statistical analysis

The data collected was entered into Microsoft Office Excel 2010 and Statistical Package for Social Sciences (SPSS version 21.0) for analysis. Descriptive statistics was used to summarize the data, with the mean and standard deviation (±SD). In addition, exploratory data analysis was conducted using median, percentage and ratios. The results were further evaluated using logistic regression, with odds ratios and 95% confidence intervals (CI) being calculated using the Stat Chart plus 5.1 software. A p-value <0.05 was considered significant.

RESULTS

In our study, we included a total of 100 participants, consisting of 50 epileptic patients and 50 controls. Among the participants, 84.0% were males and 16.0% were females. The mean age of male subjects was 24.6 years, and the mean age of female subjects was 23.1 years. The educational status of epileptic patients was matriculation, and they had a positive family history of neurological abnormalities and diabetes, as shown in Table 1. The epileptic patients had significantly elevated levels of serum TL, TC, TG, and VLDL-C as compared to controls. Additionally, HDL-C was significantly decreased in epileptic patients as compared to controls. Among the epileptic patients, male patients had significantly higher levels of TL, TC, TG, and VLDL-C as compared to their female counterparts. There was a significant rise in serum LDL-C, TG, and VLDL-C in the 36-45 age group as compared to the other age groups, as shown in Table 2. Those patients who were taking Episenta (a combination of sodium and valproic acid) showed significantly higher TC. Whereas, non-significantly higher levels of serum TL, TG , LDL-C , and VLDL-C , while their HDL-C levels were lower in Epival drug users. There was a significant difference in the concentrations of total cholesterol among patients who were taking the Epival (Figure 1).

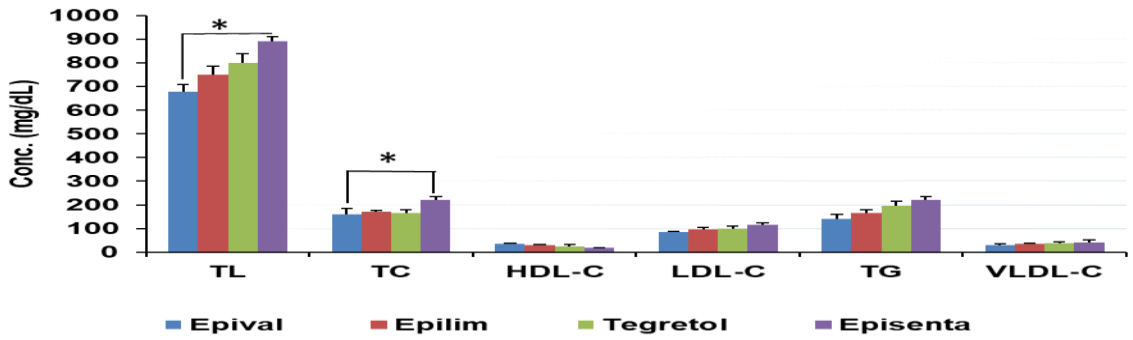

Figure: 1 Antiepileptic drug effects on lipid profile in epileptic patients

Table: 1 Socio-demographic characteristic of epileptic patients and controls.

Characteristics	Epileptic Patients N=50 (%)	Controls N=50 (%)
Gender		
Male	84.0	84.0
Female	16.0	16.0
Age groups(Year)		
15-25	64.0	64.0
26-35	22.0	22.0
36-45	10.0	10
>46	4.0	4.0
Marital Status		
Married	38.0	32.0
Unmarried	62.0	68.0
Occupation		
Government Job	8.0	20.0
Private Job	22.0	23.0
Businessmen	25.0	32.0
Jobless	45.0	25.0
Education		
Primary	15.0	15.0
Matriculation	40.0	30.0
Intermediate	18.0	20.0
Graduation	17.0	30.0
Diploma	10.0	5.0
Comorbidities		
Hypertension	20.0	15.0
Diabetes	15.0	35.0
Hepatitis	25.0	30.0
Heart Disease	10.0	15.0
Neurological disorder	30.0	5.0

Table: 2 Gender and gender wise comparison of lipid profile in epileptic patients and controls.

Parameters	TL Range (450-850)mg/dL Mean ± SD	TC Range (<200) mg/dL Mean ± SD	HDL-C Range (45-55) mg/dL Mean ± SD	LDL-C Range (<130) mg/dL Mean ± SD	TG Range (<200) mg/dL Mean ± SD	VLDL-C Range (15-25) mg/dL Mean ± SD
Epileptic Patients (n=50)	742.84 ± 30.8	165 ± 16.18	30.95 ± 10.96	91.92 ± 15.92	166.04 ± 16.04	32.94 ± 12.86
Controls (n=50)	623 ± 25..86	140.44 ± 20.45	36.98± 5.7	84.9 ± 7.48	129.38 ± 15.6	25.86 ± 6.7
P-value (<0.05)	0.003	0.008	0.0003	0.06	0.0028	0.004
Male Epileptic patients (n=42)	768.64 ± 40.7	171.07 ± 30.66	30.35 ± 7.35	94.47 ± 17.73	172.52 ± 25.6	34.21 ± 16.53
Female Epileptic patients (n=08)	607.37±30.42	134.25±18.54	34.12±6.35	78.5±14.6	132±17.66	26.25±3.38
P-value (<0.05)	0.002	0.0025	0.21	0.028	0.007	0.008
15-25 years(n=33)	662.51 ± 98.5	134.25 ± 18.54	33.66 ± 8.47	83.39 ± 15.82	137.42 ± 33.44	27.12 ± 7.01
26-35 years(n=10)	742.84 ± 85.5	145.75 ± 30.96	30.96 ± 9.92	91.92 ± 20.72	166.04 ± 76.57	32.94 ± 15.48
36-45 years(n=05)	1049.8 ± 99.53	165.18 ± 54.16	19.6 ± 10.48	118.2 ± 25.65	285.2 ± 95.64	57.19 ± 141.58
≥46 years (n=02)	1040.34±249.3	232.73 ± 96.48	25.10 ± 10.18	107.5 ± 22.5	107.5 ± 22.5	52.17 ± 30.52
P-value (<0.05)	0.61	0.002	0.003	0.005	0.001	0.006

(P-value <0.05), TL=Total Lipid, TC= Total Cholesterol, HDL-C= High Density Lipoprotein, LDL-C Low Density Lipoprotein, TG= Triglycerides, VLDL-C Very low density lipoprotein.

DISCUSSION

A total of 50 epileptic patients and 50 controls participated in this study. There was male predominance of male epileptic patients than female epileptic patients. This finding was consistent with previously reported studies, where A. Gholami *et al.* (2016) and Bano *et al*. (2015), showed more males than females suffering from epilepsy (8, 9). We divided participants into age groups and found that the majority of epileptic patients were 15-25 years age, as reported earlier by Svalheim *et al*., (2017) that the majority of patients with epilepsy were in the age group 18-35 years with an average age of 31.5 years (10).

These findings suggest that epilepsy, as well as gender and age, may influence the lipid profile of patients, and highlights the need for appropriate management of the cardiovascular health of patients with epilepsy. Antiepileptic medication therapy duration and lipid profile were found to be significantly correlated. Zenteno et al. (2007) conducted a study on comorbidities in epileptic patients and found that the majority of patients had neurological disorders, which is consistent with the results of current study. Mintzer et al. (2016) reported that epileptic patients who were taking antiepileptic drugs had higher levels of TL, TG, and VLDL-C as compared to controls. Similarly, several other studies have also reported elevated levels of TC, TG, HDL-C, and LDL-C, which are comparable with current findings. These studies provide further evidence of the impact of epilepsy and its treatment on serum lipid levels in patients, and highlight the importance of monitoring and managing the cardiovascular health of patients with epilepsy (11, 12) . Another study conducted by

Mintzer et al. (2018) reported that epilepsy patients had higher serum lipid levels compared to controls, and HDL-C levels were significantly lower in epilepsy patients (13, 14,15).
Mugloo et al. (2017) reported an increase in TL, TC, TG, and LDL-C levels in epileptic patients who were using antiepileptic drugs. They also found that the concentration of VLDL-C was not significantly high in antiepileptic drug users. However, other investigators have reported a negative association between the use of antiepileptic drugs and serum lipid profile (16, 17). These findings further emphasize the impact of specific epilepsy medications on the serum lipid profile of patients and the importance of monitoring their cardiovascular health regularly.
Shah et al. (2016) conducted a study on the lipid profile of patients with epilepsy and found that gender played a significant role in determining the lipid profile. Their findings indicated that male patients with epilepsy had significantly higher levels of serum TL, TC, TG, and VLDL-C when compared to female patients with epilepsy. On the other hand, the levels of HDL-C were found to be higher in female patients with epilepsy than in male patients. These results suggest that gender differences may influence the lipid profile of patients with epilepsy and should be taken into consideration when assessing and managing the cardiovascular health of patients with epilepsy (11).
According to the findings of present study, which is aligned with the research conducted by Irem Fatima et al. in 2009, who reported that male patients with epilepsy have been shown to exhibit higher levels of TC and LDL-C when compared to female patients with epilepsy. This suggests that male patients with epilepsy may be at a higher risk of developing cardiovascular diseases than their female counterparts. However, the same study also revealed that male epileptic patients had higher levels of HDL-C than female epileptic patients, indicating a potential protective effect of HDL-C against the development of cardiovascular disease in male patients with epilepsy (18, 19).
Patients who use Episenta showed significantly higher levels of TC, TL, LDL-C, TG, and VLDL-C when compared to those who were not using Episenta. Conversely, the levels of HDL-C were found to be lower in Episenta users than non-users. The results of our study partially agree with the findings of a previous study conducted by Mintzer et al. (2013), which demonstrates that carbamazepine can significantly reduce serum total cholesterol. While our findings align with Mintzer's results in terms of the reduction in HDL-C levels, they differ in terms of TC and LDL-C levels, which were found to be higher in our study among patients who use Episenta (20). This was a prospective study from patients taking antiepileptic drugs, thus it is the strength of the study, however a small sample size and the 1:1 ratio of cases and controls is taken as a limitation of the study.

CONCLUSION

Antiepileptic drugs significantly alter the serum lipid levels in patients with epilepsy. It is worth noting that the normal ranges for serum cholesterol and its fractions are wide and may vary depending on factors such as gender and age. Specifically, male epileptic patients have higher lipid profiles as compared to female epileptic patients. Regular monitoring of serum lipid levels appears to be essential for patients undergoing such therapy and proper diet management may reduce the risk of associated clinical manifestations.

Conflict of interest:

Authors declare no conflict of interest

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REFERENCES

1. Adhimoolam M, Arulmozhi R. Effect of antiepileptic drug therapy on thyroid hormones among adult epileptic patients: An analytical cross-sectional study. Journal of Research in Pharmacy Practice. 2016;5(3):171.
2. Petty SJ, O'brien T, Wark J. Anti-epileptic medication and bone health. Osteoporosis international. 2017;18(2):129-42.
3. Menon B, Harinarayan C. The effect of anti epileptic drug therapy on serum 25-hydroxyvitamin D and parameters of calcium and bone metabolism—A longitudinal study. Seizure. 2017;19(3):153-8.
4. Ngugi AK, Bottomley C, Kleinschmidt I, Sander JW, Newton CR. Estimation of the burden of active and life-time epilepsy: a meta-analytic approach. Epilepsia. 2010;51(5):883-90.
5. Beydoun A, DuPont S, Zhou D, Matta M, Nagire V, Lagae L. Current role of carbamazepine and oxcarbazepine in the management of epilepsy. Seizure. 2020;83:251-63.
6. Nabbout R, Camfield CS, Andrade DM, Arzimanoglou A, Chiron C, Cramer JA, et al. Treatment issues for children with epilepsy transitioning to adult care. Epilepsy & Behavior. 2017;69:153-60.
7. Nag T, Ghosh A. Cardiovascular disease risk factors in Asian Indian population: A systematic review. Journal of cardiovascular disease research. 2019;4(4):222-8.
8. Gholami A, Salarilak S, Lotfabadi P, Kiani F, Rajabi A, Mansori K, et al. Quality of life in epileptic patients compared with healthy people. Medical journal of the Islamic Republic of Iran. 2016;30:388.
9. Rafiq M, Bano S, Tariq PATA. Effects of antiepileptic drug therapy on 25OH Vitamin D levels. Pakistan Journal of Physiology. 2015;11(4):24-6.
10. Svalheim S, Sveberg L, Mochol M, Taubøll E. Interactions between antiepileptic drugs and hormones. Seizure. 2017;28:12-7.
11. Mintzer S, Miller R, Shah K, Chervoneva I, Nei M, Skidmore C, et al. Long-term effect of antiepileptic drug switch on serum lipids and C-reactive protein. Epilepsy & Behavior. 2016;58:127-32.
12. Mintzer S, Miller R, Shah K, Chervoneva I, Nei M, Skidmore C, et al. Long-term effect of antiepileptic drug switch on serum lipids and C-reactive protein. Epilepsy & Behavior. 2018;58:127-32.
13. Manimekalai K, Visakan B, Salwe KJ, Murugesan S. Evaluation of effect of antiepileptic drugs on serum lipid profile among young adults with epilepsy in a tertiary care hospital in Pondicherry. Journal of Clinical and Diagnostic Research: JCDR. 2015;8(8):HC05.
14. Yilmaz E, Dosan Y, Gurgoze M, Gungor S. Serum lipid changes during anticonvulsive treatment. Serum lipids in epileptic children. Acta neurologica belgica. 2013;101(4):217-20.
15. Mintzer S, Trinka E, Kraemer G, Chervoneva I, Werhahn KJ. Impact of carbamazepine, lamotrigine, and levetiracetam on vascular risk markers and lipid-lowering agents in the elderly. Epilepsia. 2018;59(10):1899-907.

16. Mugloo MM, Akhtar R, Malik S. Assessment of serum lipid profile and liver function parameters in children with epilepsy on phenytoin or valproic acid monotherapy for 6 months and beyond. Astrocyte. 2017;3(4):180.
17. Yamamoto Y, Terada K, Takahashi Y, Imai K, Kagawa Y, Inoue Y. Influence of antiepileptic drugs on serum lipid levels in adult epilepsy patients. Epilepsy research. 2018;127:101-6.
18. Okada S, Nishina M, Koizumi K, Katayama M, Inoue S, Suga S. Impact of enzyme-inducing anti-epilepsy drugs on lipid levels in elderly patients with epilepsy. Epilepsy research. 2020;166:106428.
19. Nisha Y, Bobby Z, Wadwekar V. Biochemical derangements related to metabolic syndrome in epileptic patients on treatment with valproic acid. Seizure. 2018;60:57-60.
20. Cramer JA, Mintzer S, Wheless J, Mattson RH. Adverse effects of antiepileptic drugs: a brief overview of important issues. Expert review of neurotherapeutics. 2013;10(6):885-91.

Review Article

PHYTOCHEMICALS AND THERAPEUTIC USE OF DATE PALM (PHOENIX DACTYLIFERA L) – A NARRATIVE REVIEW

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ABSTRACT

This article provides a summary of phytochemical composition, nutritional value and health benefits of Pheonix Dactylifera L, commonly known as dates. Additionally, the article explores the potential of date fruit to be utilized as a food medicine in the treatment of various human diseases. We conducted a comprehensive review of the existing literature on the biological functions of date palm and its potential health benefits, utilizing databases literature search engines including PubMed, Scopus, Science Direct and google scholar. Regular consumption of date palm fruits (DPFs) may lower the risk of developing various chronic diseases due to its antioxidant, antidiabetic, antibacterial, anticancer and anti-mutagenic properties. Additionally, the pollen of date palm trees contains high levels of protein, fat, and carbohydrates, making it an excellent natural supplement with substantial nutritional value and energy-boosting properties. Date palm components have demonstrated potent antioxidant effects and have played a crucial role in both male and female reproductive systems, promoting fertility in both genders. Date palm pollen (DPP) has shown gonadal-stimulating potency in females and can significantly increase testosterone levels in individuals with Oligoasthenozoospermia and follicle-stimulating hormone (FSH) levels in patients with Azoospermia, making it as a potential treatment for reproductive health. According to the literature, date fruit is a highly nutritious fruit compared to other commonly consumed fruits. In conclusion dates have been shown to have a significant impact on various female reproductive parameters such as oogenesis, oocyte development, hormone modulation, and pregnancy strength.

Key Words: Date palm pollen, infertility, Phytochemicals, Phoenyx dactylifera, Azoospermia, Oligoasthenozoospermia

INTRODUCTION

In many societies, infertility is viewed negatively and considered a form of illness when there is a disruption in the reproductive system. World Health Organization (WHO) defines infertility as the inability of a couple to become pregnant after 12 months of sexual activity, without using any contraception (1). Approximately 15% of couples in their reproductive years have been reported to be

infertile after one year of consistent unprotected sexual activity, with around 10% of cases with unknown causes, globally. In specific regions of the world such as Sub-Saharan Africa, Central Asia, Eastern and Central Europe, and South Asia, the rates of infertility are higher and can even surpass 30% (2, 3). The ranges of cases have involved regional variations around the world. Infertility involves mental health issues affecting both male and females equally(4). According to research, males account for 40% of infertility cases, women for 40%, and in 20 % of cases both partners show inability to conceive (5). In Pakistan 22% of cases are reported to have infertility, out of which 4% are reportedly have secondary infertility, due to other causes. Women undergo psychological trauma as a result of social norms that associate infertility with failure on a personal, emotional, and social level (6).

GLOBAL BURDEN OF INFERTILITY

Given the rising pattern of infertility around the world, it is becoming a significant global concern in both high and low-income countries. The United States' Centers for Disease Control and Prevention (CDC) asserts that infertility has significant public health implications, extending beyond just a decline in quality of life. This includes negative consequences such as economic burden, social stigma, psychological distress, and marital problems (7). Infertility affects a significant portion of couples of reproductive age worldwide, with estimates ranging from 10-25% (48 to 180 million couples). Furthermore, infertility has shown negative impact on physical as well as mental health. This is also associated with financial difficulties, social stigma, increased risk of domestic violence, and marital instability. Both men and women are equally susceptible to infertility, but it is typically women who experience the social ramifications, particularly in societies where a woman's worth is linked to her ability to conceive and have children (8).

METHODOLOGY

The purpose of this study was to collect articles published between 2010 and 2022 that explore the relationship between Phoenix dactylifera, (date palm), and male and female infertility, as well as its role in various biological activities. To achieve this goal, several databases such as PubMed, Scopus, Web of Knowledge, Clinical Keys, Embase, Google Scholar Search Engine, Scientific Information Database (SID), and IRCT (Iranian Registry of Clinical Trials) were searched using relevant keywords. A manual search was also conducted in pertinent journal databases to ensure that no relevant articles were missed. Additionally, all references cited in review papers were examined to identify any recent relevant research. By utilizing this comprehensive search strategy, a broad range of articles related to date palm and infertility were collected and analyzed. The findings of this study will contribute to a better understanding of the potential benefits of date palm in the context of reproductive health.

THE PREVALENCE OF INFERTILITY

Infertility rate varies in gender and also across different countries, with data collected from demographic surveys not distinguishing between voluntary and involuntary infertility. In developed countries, the percentage of infertility ranges from approximately 10-18% in men and 5-10% in women, with higher rates in some countries like Finland, Switzerland, Sweden, and Canada. However, differences between countries may be attributable to the varying rates of voluntary infertility. Low-middle-income countries including Pakistan reported to have relatively higher rates of infertility, associated with minimal understanding of the condition, as well as limited access to healthcare system (6). Reported rate of infertility in Pakistan is 22%, with 18% primary infertility and secondary infertility accounting for 4%. The epidemiology of secondary infertility is not well understood (9). There is limited information available regarding the occurrence and potential causes

of secondary infertility in Pakistan. However, research indicates that unsafe practices are commonly used by healthcare providers and women during childbirth and the postpartum period, leading to pelvic inflammatory disease (PID), tubal blockages, and ultimately resulting in infertility (10). This raises the rate of infertility among women.

CAUSES OF INFERTILITY

Various factors contribute to infertility and can vary depending on the region of the world. However, common determinants across most areas include lifestyle factors, epidemic infections, sexually transmitted diseases, and nutritional deficiencies (11). Changes in sexual behavior and the elimination of restrictions, as well as lifestyle factors such as smoking and alcohol consumption, can affect sperm quality. Historically, research on infertility has focused on various factors, including issues related to ovulation (accounting for 20% of infertility cases), utero-tubal peritoneal factors (accounting for 30% of cases), sperm migration issues (accounting for 10% of cases), and male factor infertility (accounting for 30% of cases) (12). 15% of male and 10% of female infertile may have genetic abnormalities, such as chromosome aberrations and single gene mutations (13). There are three primary pathological factors that can affect a woman's fertility: endometriosis, congenital or acquired uterine abnormalities, and post-infectious tubal damage. Congenital issues, such as a septate uterus, and acquired conditions like myomas and synechiae can lead to infertility, miscarriage, and other obstetric complications. Additionally, medical conditions such as thyroid disorders and diabetes can also contribute to fertility issues (14). The most common cause of tubal injury is pelvic inflammatory disease (15). Unhealthy lifestyle choices, including poor eating habits, stress, drinking alcohol, smoking, and obesity, can have negative impacts on a person's overall health and reproductive ability. These factors have been found to significantly decrease the likelihood of pregnancy in women. The WHO distinguishes between primary infertility, which refers to a woman's inability to conceive, and secondary infertility, which occurs when a woman has previously had at least one successful pregnancy in her marriage but is unable to conceive again (16). Primary infertility accounts for 57.5% of instances compared to secondary infertility's 42.5% (17).

Figure: 1 Risk factors of infertility.

DATE PALM

Date palm tree, botanically known as Phoenyx dactylifera is a member of the family Arecaceae (palms), subfamily Coryphoideae and order Arecales, monocotyledonous. It is perennial tree (18). The plant is of medium size and can grow either individually or in clusters with multiple branches stemming from a single root system. Its flower is the primary source of economic value. The plant typically reaches a height of 15 to 25 meters, and its leaves are pinnate, measuring around 4 to 6 meters in length and featuring approximately 150 leaflets with spines on the petiole. The leaflets themselves are 2 centimeters wide and 30 centimeters long. The plant's full crown spans can vary from 6 to 10

meters (19). The date palm, one of the oldest fruit crops in the world, is primarily cultivated for its highly nutritious fruits, which serve as a staple food in many countries, particularly in the Gulf region. In Pakistan, the date palm is the third most important fruit crop, following citrus and mango. It is cultivated on approximately 90,000 acres of land across the country's four provinces, yielding an annual production of roughly 600,000 metric tons (20).

CHEMICAL COMPONENTS OF DATE PALM

Dates contain varying amounts of phytochemicals, including minerals, flavonoids, phenolics, carotenoids, and vitamins, making them a valuable source of bioactive and functional compounds with potential medicinal benefits. These compounds provide the body with essential energy and may also act as effective therapeutic agents against a range of diseases (21). Depending on size and species, date palm fruit has 20–70 calories and is abundant in carbohydrates (70%) with sugars making up the majority of those calories (88% in certain types) (19). Date fruits are a significant source of vitamins and mineral salts. Among the ten minerals found in dates, the most abundant are selenium, copper, potassium, and magnesium. A 100-gram serving of dates can supply 15% of daily requirements of these minerals. Dates have been reported to be a source of both vitamins B-complex and vitamin C which are essential vitamins for human body for different functions. Additionally, they are rich in dietary fiber, providing approximately 8.0 grams of fiber per 100 grams of dates. The majority of this fiber is insoluble (22).

Dates also contain tocopherols, carotenoids, and polyphenols, including flavonoids and tannins, which possess various biological properties, such as antibacterial and antioxidant activities. Phenolic compounds found in dates have been shown to reduce oxidative stress associated with chronic diseases, including heart disease, neurodegenerative disorders, cancers, and diabetes.

Date palm pits are a rich source of non-reducing sugar, with a composition of 3.82% glucose and 1.68% of fructose. In general, 100g of dates provide 5.1g of proteins, 9.0g of fat, and 73.1g of fiber. The fat content of fresh dates is 0.14 g per 100 g, while dried dates contain 0.38 g/100 g. Additionally, date palm pits are rich in phenolic compounds, with a content of 3942 mg/100g (23). The values of these nutrients may vary according to the differences in cultivation, evaporation conditions, and assessment test methods applied (24).

The carotenoid content of dates is reported to 913 g/100 g and 973 g/100 g in fresh and dry dates respectively. The total carotenoid content varies in yellow and red varieties of dates. While phenol contents differ between fresh (i.e. 193.7 mg/100 g) and dried dates (i.e. 239.5 mg/100 g). Different types of dried dates may have varying in amounts of phenolic compounds (25). The extensive use of the date palm in botany and medicine highlights its significance in promoting human health. Clinical studies have demonstrated various benefits associated with the date palm (28). The leaves, fruits, pits, and pollen of the plant have been used to prevent and treat diverse medical conditions (29). These components serve as the primary source of easily accessible bioactive compounds that are responsible for their biological activities. Historically, the date palm has been employed in addressing issues with the reproductive and endocrine systems. Figure 2 illustrates the impact of the date palm and its constituents on male and female reproductive systems. The potent antioxidant properties of date fruits are vital in enhancing fertility in both men and women (30).

Organisms typically do not require bioactive chemicals for their daily activities as they are naturally generated as secondary metabolites that modulate metabolic processes (31). Date palm fruits contain two types of bioactive molecules: nutritive and non-nutritive bioactive chemicals (32-34). Date Palm

fruits contain quickly absorbed carbohydrates such as glucose and fructose, which have no adverse effects on triglycerides and blood sugar levels when consumed by healthy individuals (35). Dates also contain Non Starch Polysaccharides (NSPs) that provide approximately one-fourth of the daily NSP requirement in nine dates per day (36, 37). NSPs play a crucial role in improving gastrointestinal function and regulating digestion, making dates palm fruits a natural laxative that promotes regular bowel movements (32, 38, 39).

Table 2 The nutritional composition of different parts of date palm.

Date Palm Parts	Nutritional Composition	References
Date leaves	On a dry weight basis, the nutritional composition of this substance includes crude protein (4.8%), crude fiber (31.9%), and ash (12.9%), with an average calcium content of about 7 g/kg and phosphorus content of about 1 g/kg.	(26)
Date seed	The moisture, protein, fat, ash, and dietary fiber content of this substance ranges from 3.1-7.1%, 2.3-6.4%, 5.0-13.2%, 0.9-1.8%, and 22.5-80.2%, respectively. It also contains phenolics (3102-4430 mg gallic acid equivalents/100 g), antioxidants, and dietary fiber (78-80 g/100 g).	(27)
Palm pollen grains	The substance has a moisture content of 28.80%, ash content of 4.57%, crude fiber content of 1.37%, crude fat content of 20.74%, protein content of 31.11%, and carbohydrate content of 13.41%.	(27)

Figure: 2 Effects of date palm on male and female reproductive system.

BIOLOGICAL POTENTIAL OF DATEPLAM

Date palm fruit is well known for its beneficial nutritional properties for human consumption and health. Cultivars with a variety of bioactive ingredients may significantly reduce the risk of oxidation of vital biological macromolecules (40). Phenolic chemicals have been associated with a variety of biological processes. Thus, research on humans has clearly shown that polyphenols have medicinal potential. The latter has an antimicrobial and antioxidant effect and prevents lipid peroxidation, anti-carcinogenic and platelet aggregation (41).

Antibacterial and Antifungal activity of date palm

Many plants commonly found in our diets have shown potential to prevent and/or treat various infectious diseases and various health conditions. In vitro study by Al-Alawi and colleagues have demonstrated that date palm fruits have antibacterial, antifungal, antioxidant, and anti-mitotic activities (42).

Various components of Phoenix dactylifera, including dried leaves, fruits, seeds, and tree bark, were extracted using water, methanol, and acetone, and their antibacterial efficacy against Staphylococcus

aureus, Streptococcus pyogenes, Escherichia coli, and Pseudomonas aeruginosa was evaluated. All parts of the tree showed some degree of antimicrobial activity, however, the fruit extract showed the highest antibiotic potential as compared to the other parts of the tree (43). Some of organic extracts and phenolic substances of date seeds and pollen, are identified in tissue of date seeds, have shown considerable antibacterial properties against both gram positive and gram negative bacteria (44).

Date extract is effective against Candidiasis infections, which is caused by Candida albicans, a significant and well-known Candida yeast species that results in fungal infections in the gynecological and digestive mucosa. The research has shown that the flavonoids in date extracts have an antifungal impact on Candida albicans in vitro, leading to its deformation, weakness, and partial cell collapse (45).

Antioxidant activity of date palm

Date palm fruits are reported to have the highest levels of antioxidants, as compared to strawberries, kiwis, guava, white pomegranates, and purple mulberries (46). Though, the antioxidant capacity of date palm fruits is influenced by a number of factors such as the variety of dates, ripeness, and processing (47, 48). Kriaa et al. examined the phenolic content and antioxidant capacity of three different date palm leaf varieties and found that all extracts exhibited antioxidant and radical-scavenging activity, albeit to varying degrees (49). Chaira et al. attributed the high antiradical activity of the Tunisian Korkobbi variety to its high flavonoid content (50). Moreover, the overall antioxidant activity of dates was observed to decrease after sun drying and storing, which may be due to oxidation or the breakdown of the antioxidants such as tannins become insoluble after drying (51).

Anti-cancer and Anti-mitotic activity of Date palm

Due to their high reactivity, free radicals contribute to the activation of cancer-causing substances by harming live tissue through cellular oxidation processes (33). Furthermore, it has been found that the anticancer effects of date palm fruits components are correlated with the presence of β–glucans (52). Date palm fruits components also have anti-mutagenic qualities because they inhibit mutagenicity. The presence of bioactive chemicals, including anthocyanin, phenolic acids, selenium, and the beta-carotene present in date palm fruits is what constitutes this type of activity (53).

Antidiabetic Significance of Date Palm.

Although date palm fruits are rich in monosaccharides (i.e. glucose and fructose), therefore ideally diabetic patients should limit or avoid their consumption. Although there is no strong evidence available showing link of poor glycemic control of development of diabetes (36). The role of date palm fruits components in diabetes management is still uncertain. Nonetheless, a study on alternative sweeteners reported that granulated date sugar has potential antidiabetic properties, making it a natural replacement sweetener for diabetic patients (54). This antidiabetic action may be due to the presence of phenolic compounds that inhibit α-glucosidase and α-amylase activity, which suppresses carbohydrate digestion and reduces the amount of glucose absorbed from the small intestine.

ROLE OF DATE PALM IN FERTILITY

Date palm pollen, which has a high amount of protein, fat, and carbohydrates, stimulates the male reproductive cells. The amino acids glycine glutamine, leucine, tyrosine, phenylalanine, aspartic acid, threonine, arginine, histidine, lysine, proline, methionine, isoleucine, serine, valine, and alanine are the main components of date pollen. Moreover, pollen is an abundant supply of vital vitamins, including vitamin A, vitamins C, E and vitamin B (thiamine, riboflavin, biotin, and folic acid). As a result, pollen should be emphasized as an appropriate natural supplement that provides energy and

has significant nutritional value (55). Traditionally, it was thought to be an fertility enhancer in males thus considered as natural male fertility supplement (30). The presence of estrogens hormone may be the cause of date palm pollen aphrodisiac effects. Date palm pollen has shown gonadal stimulating potency and reproductive promotion actions in women, demonstrating that its pharmacological effects are not just limited to males. Date palm pollen may also significantly increase testosterone levels in individuals with Oligoasthenozoospermia and follicle-stimulating hormone (FSH) levels in patients with azoospermia, as well as be used to treat sexual weakness and incapacity in the Arab world (56). Additionally, date seeds may increase testosterone levels, blood biochemical parameters, and testis antioxidant status (57). Many studies have been conducted to demonstrate the impact of date palm components on variables related to male fertility (58). The reports have shown that date seeds improve testosterone level, and also antioxidant status in testis thus improving male reproductive capacity (59) (Table 2).

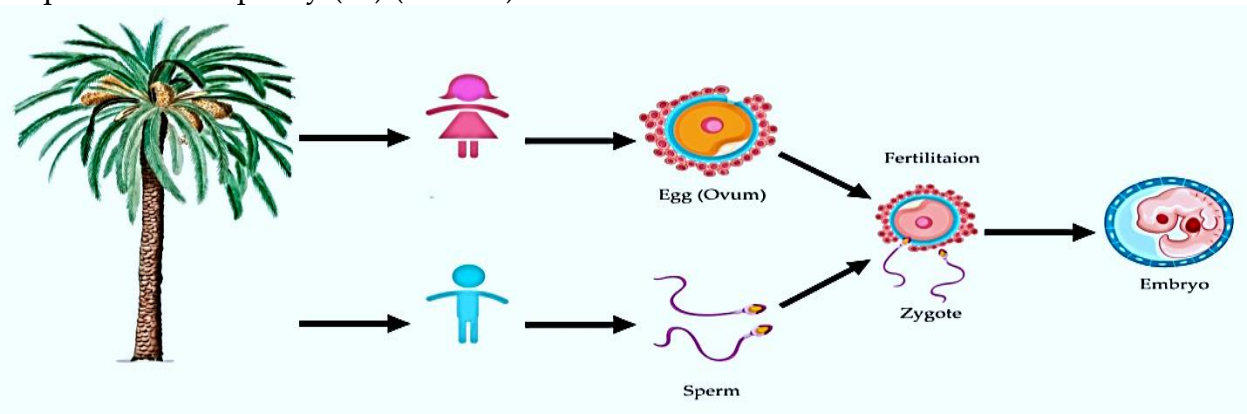

Figure: 3 A diagrams showing how the date palm affects sexual reproduction.

Earlier report has shown effect of DPP to increase concentrations of estradiol and testosterone resulting in an increased epididymis-body weight ratio (71). In another study, infertile patients were given capsules containing 500mg of dried date palm pollen twice daily for three months, which resulted in a significant increase in their sperm counts. This can be attributed to the presence of a gonadotropic active chemical in the DPP. The pollen also contains steroid precursors that may increase the synthesis of testosterone, thereby explaining the rise in testosterone levels (72). In addition, there is also evidence available which has suggested effects of DPP on sexual interactive parameters of male adult rats. The pollen was influencing weight of testicles and also testosterone production thus increasing serum testosterone levels. Additionally, Mehraban et al. conducted a study to determine how DPP extracts affect male rat reproductive parameters. DPP was administered in dosages of 120 and 240 mg/kg, and their results showed that DPP enhances fertility factors. (73). This suggests that DPP has potential to improve male fertility and sexual activities. However, most of the literature reported on animal models in particular rats and mice, limited literature available on human subjects.

CONCLUSIONS

Dates are a rich source of various nutrients, including phytochemicals, saponins, tannins, carotenoids, minerals, and vitamins, which have numerous biological functions in the body. Date palm fruits (DPFs) are found to have the highest antioxidant activity compared to other fruits, making them a potential dietary intervention for individuals with metabolic syndrome and related diseases such as diabetes, CHD, and stroke. Date palm has also been shown to have a positive impact on fertility by

increasing testosterone and FSH levels in oligoasthenozoospermia patients and regulating female reproductive parameters, such as oogenesis and pregnancy. Although most studies have been conducted on rats and mice, more research is required to establish the efficacy of date palm products in treating infertility in humans. This review highlights the phytochemical and pharmacological properties of DPF and its potential use in treating fertility disorders.

Table 2. The bioactive components of date palm and their mechanism.

Date and Date Parts	Active Components	Mechanism	References
Date fruit	Simple sugar	Source of energy for mother's during labor.	(60)
Date fruit	Glucose	Provide energy, strengthens uterine muscles, and nutritional supplement for cervical dilutions	(61)
Date fruit	Calcium	Helps in smooth muscle contraction of the uterus during labor	
Date fruit	Tannin	Helps in smooth muscle contractions of cervix. Tannin and Linoleic acid help in control of bleeding	(62)
Date fruit	Folic acid	Essential for cell division and genetic structure maintenance	(63)
Date fruit	Sugar, Vitamin B1, and Iron	Control uterus movements	(64)
Date fruit	Tannin and Linoleic acid	Control bleeding	(59)
Date fruit	Potuchin hormone	Help to reduce postpartum bleeding	(64)
Date Palm Pollens	Estrogen compounds	Animal model studies suggest effect of estrogen on mice reproductive system	(59)
Date Palm Pollens	Estrogenic compound: estradiol, estriol, and estrone	Gonadotrophic activity in male rats affecting reproductive system	(65)
Date Palm Pollens	Carbohydrates, Saponins and gallic tannins,	Improved male reproductive parameters in mouse models	(66)
Date Palm Pollens	Saponins	Stimulate testosterone production from testes	(67)
Date Palm Pollens	Estradiol components	Helps in spermatogenesis and male reproductive tissue regeneration	(68)
Date Palm Pollen grains	Phytochemicals: alkaloids, saponins, and flavonoids	Improve sexual behaviors in male rat by enhancing androgenic activity.	(69)
Date Palm Pollen grains extracts	Estrogenic materials	Improve male infertility by stimulating gonads	(70)

Conflict of Interest

Authors declare that there is no conflict of interest.

REFRENCES

1. Antonelli M, Donelli D, Firenzuoli F. Therapeutic efficacy of orally administered pollen for nonallergic diseases: An umbrella review. Phytotherapy Research. 2019;33(11):2938-47.
2. Taha EA, Sabry M, Abdelrahman IFS, Elktatny H, Hosny A. Impact of irregular marital cohabitation on quality of life and sexual dysfunction in infertile men from upper Egypt. Clinical and Experimental Reproductive Medicine. 2020;47(1):77.
3. Inhorn MC, Patrizio P. Infertility around the globe: new thinking on gender, reproductive technologies and global movements in the 21st century. Human reproduction update. 2015;21(4):411-26.
4. Direkvand Moghaddam A, Delpisheh A, Sayehmiri K. An Investigation of the Worldwide Prevalence of Infertility As a Systematic Review. Qom Univ Med Sci J. 2016;10(1):76-87.
5. Agarwal A, Mulgund A, Hamada A, Chyatte MR. A unique view on male infertility around the globe. Reproductive biology and endocrinology. 2015;13(1):1-9.
6. Ahmed HM, Khan M, Yasmin F, Jawaid H, Khalid H, Shigri A, et al. Awareness regarding causes of infertility among out-patients at a tertiary care hospital in Karachi, Pakistan. Cureus. 2020;12(4).
7. Medicine PCotASfR. Definitions of infertility and recurrent pregnancy loss: a committee opinion. Fertility and sterility. 2018;99(1):63.
8. Thoma M, Fledderjohann J, Cox C, Adageba RK. Biological and social aspects of human infertility: a global perspective. Oxford research encyclopedia of global public health2021.
9. Sami N, Ali TS, Wasim S, Saleem S. Risk factors for secondary infertility among women in Karachi, Pakistan. PloS one. 2019;7(4):e35828.
10. Shahzad H, John A, Ali A, Ashraf A, Naeem MA. Incidence of infertility in females and Evaluation of its Causes Using Ultrasonography: Incidence and Causes of Infertility in Females. Pakistan BioMedical Journal. 2022:55-8.
11. Petraglia F, Serour GI, Chapron C. The changing prevalence of infertility. International Journal of Gynecology & Obstetrics. 2013;123:S4-S8.
12. Anwar S, Anwar A. Infertility: A review on causes, treatment and management. Womens Health Gynecol. 2016;5:2-5.
13. Miyamoto T, Minase G, Okabe K, Ueda H, Sengoku K. Male infertility and its genetic causes. Journal of Obstetrics and Gynaecology Research. 2015;41(10):1501-5.
14. Codner E, Merino P, Tena-Sempere M. Female reproduction and type 1 diabetes: from mechanisms to clinical findings. Human reproduction update. 2012;18(5):568-85.
15. Abrao MS, Muzii L, Marana R. Anatomical causes of female infertility and their management. International Journal of Gynecology & Obstetrics. 2013;123:S18-S24.
16. Tabong PT-N, Adongo PB. Infertility and childlessness: a qualitative study of the experiences of infertile couples in Northern Ghana. BMC pregnancy and childbirth. 2013;13(1):1-10.
17. Deshpande PS, Gupta AS. Causes and prevalence of factors causing infertility in a public health facility. Journal of human reproductive sciences. 2019;12(4):287.
18. Laouini SE. A COMPARATIVE STUDY OF THE ANTIOXIDANT ACTIVITY AND PHYTOCHEMICAL COMPOSITION OF LEAVES EXTRACT OF SOME VARIETIES OF DATE PALM.
19. Ahmad A, Soni Dutta S, Varun Singh K, Santosh MK. PHOENIX DACTYLIFERA LINN.(PIND KHARJURA): A REVIEW. International Journal of Research in Ayurveda & Pharmacy. 2019;4(3).
20. Abul-Soad AA, Mahdi SM, Markhand GS. Date Palm Status and Perspective in Pakistan. In: Al-Khayri JM, Jain SM, Johnson DV, editors. Date Palm Genetic Resources and Utilization: Volume 2: Asia and Europe. Dordrecht: Springer Netherlands; 2015. p. 153-205.

21. Younas A, Naqvi SA, Khan MR, Shabbir MA, Jatoi MA, Anwar F, et al. Functional food and nutra-pharmaceutical perspectives of date (Phoenix dactylifera L.) fruit. Journal of food biochemistry. 2020;44(9):e13332.
22. Al-Farsi MA, Lee CY. Nutritional and functional properties of dates: a review. Critical reviews in food science and nutrition. 2018;48(10):877-87. Epub 2008/10/25.
23. Masmoudi-Allouche F, Touati S, Mnafgui K, Gharsallah N, El Feki A, Allouche N. Phytochemical profile, antioxidant, antibacterial, antidiabetic and anti-obesity activities of fruits and pits from date palm (Phoenix dactylifera L.) grown in south of Tunisia. Journal of Pharmacognosy and Phytochemistry. 2016;5(3):15-22.
24. Idowu AT, Igiehon OO, Adekoya AE, Idowu S. Dates palm fruits: A review of their nutritional components, bioactivities and functional food applications. AIMS Agriculture and Food. 2020;5(4):734-55.
25. Nasir MU, Hussain S, Jabbar S, Rashid F, Khalid N, Mehmood A. A review on the nutritional content, functional properties and medicinal potential of dates. Sci Lett. 2015;3(1):17-22.
26. Shehzad M, Rasheed H, Naqvi SA, Al-Khayri JM, Lorenzo JM, Alaghbari MA, et al. Therapeutic potential of date palm against human infertility: A review. Metabolites. 2021;11(6):408.
27. Shehzad M, Rasheed H, Naqvi S, Al-Khayri J, Lorenzo J, Alaghbari M, et al. Therapeutic Potential of Date Palm against Human Infertility: A Review. Metabolites 2021, 11, 408. s Note: MDPI stays neu-tral with regard to jurisdictional claims in …; 2021.
28. Echegaray N, Pateiro M, Gullon B, Amarowicz R, Misihairabgwi JM, Lorenzo JM. Phoenix dactylifera products in human health–A review. Trends in Food Science & Technology. 2020;105:238-50.
29. Rivera D, Obón C, Alcaraz F, Laguna E, Johnson D. Date-palm (Phoenix, Arecaceae) iconography in coins from the Mediterranean and West Asia (485 BC–1189 AD). Journal of Cultural Heritage. 2019;37:199-214.
30. Abdi F, Roozbeh N, Mortazavian AM. Effects of date palm pollen on fertility: research proposal for a systematic review. BMC research notes. 2017;10(1):1-4.
31. Livesey G, Taylor R, Livesey HF, Buyken AE, Jenkins DJ, Augustin LS, et al. Dietary glycemic index and load and the risk of type 2 diabetes: a systematic review and updated meta-analyses of prospective cohort studies. Nutrients. 2019;11(6):1280.
32. Freha G, Fatma M, Meriem D, Cherifa H. Effect of Algerian varieties dates on glycemic, arterial blood pressure and satiety responses. Asian Journal of Pharmaceutical Research and Health Care. 2016;8(2).
33. Siddiq M, Aleid SM, Kader AA. Dates: postharvest science, processing technology and health benefits: John Wiley & Sons; 2013.
34. Kacem I, Martinez-Saez N, Kallel F, Ben Jeddou K, Boisset Helbert C, Ellouze Chaabouni S, et al. Use of almond shell as food ingredient. European Food Research and Technology. 2017;243(12):2115-26.
35. Rock W, Rosenblat M, Borochov-Neori H, Volkova N, Judeinstein S, Elias M, et al. Effects of date (Phoenix dactylifera L., Medjool or Hallawi Variety) consumption by healthy subjects on serum glucose and lipid levels and on serum oxidative status: a pilot study. Journal of agricultural and food chemistry. 2019;57(17):8010-7.
36. Al-Mssallem M. Research article consumption of dates among Saudi adults and its association with the prevalence of type 2 diabetes. Asian J Clin Nutr. 2018;10:58-64.
37. Al-Mssallem MQ, Elmulthum NA, Elzaki RM. Nutritional security of date palm fruit: an empirical analysis for Al-Ahsa region in Saudi Arabia. Scientific Journal of King Faisal University. 2019;20:47-54.
38. Evans RA, Frese M, Romero J, Cunningham JH, Mills KE. Fructose replacement of glucose or sucrose in food or beverages lowers postprandial glucose and insulin without raising triglycerides: a systematic review and meta-analysis. The American journal of clinical nutrition. 2017;106(2):506-18.
39. Samad MA, Hashim SH, Simarani K, Yaacob JS. Antibacterial properties and effects of fruit chilling and extract storage on antioxidant activity, total phenolic and anthocyanin content of four date palm (Phoenix dactylifera) cultivars. Molecules. 2016;21(4):419.

40. Bentrad N, Hamida-Ferhat A. Date palm fruit (Phoenix dactylifera): Nutritional values and potential benefits on health. The Mediterranean Diet: Elsevier; 2020. p. 239-55.
41. Taleb H, Maddocks SE, Morris RK, Kanekanian AD. Chemical characterisation and the anti-inflammatory, anti-angiogenic and antibacterial properties of date fruit (Phoenix dactylifera L.). Journal of ethnopharmacology. 2016;194:457-68.
42. ALrajhi M, Al-Rasheedi M, Eltom SEM, Alhazmi Y, Mustafa MM, Ali AM. Antibacterial activity of date palm cake extracts (Phoenix dactylifera). Cogent Food & Agriculture. 2019;5(1):1625479.
43. Al-Daihan S, Bhat RS. Antibacterial activities of extracts of leaf, fruit, seed and bark of Phoenix dactylifera. African Journal of Biotechnology. 2012;11(42):10021-5.
44. Bentrad N, Gaceb-Terrak R, Benmalek Y, Rahmania F. Studies on chemical composition and antimicrobial activities of bioactive molecules from date palm (Phoenix dactylifera L.) pollens and seeds. African journal of Traditional, Complementary and alternative Medicines. 2017;14(3):242-56.
45. Tsai P-W, Chen Y-T, Hsu P-C, Lan C-Y. Study of Candida albicans and its interactions with the host: a mini review. BioMedicine. 2013;3(1):51-64.
46. Guo C, Yang J. Antioxidant activities of Ferula assa-foetida as determined by FRAP assay. Nutr Res. 2013;23(12):1719-26.
47. Al-Alawi RA, Al-Mashiqri JH, Al-Nadabi JS, Al-Shihi BI, Baqi Y. Date palm tree (Phoenix dactylifera L.): natural products and therapeutic options. Frontiers in plant science. 2017;8:845.
48. Siddiq M, Aleid SM, Kader AA. Dates: postharvest science, processing technology and health benefits: John Wiley & Sons; 2016.
49. Kriaa W, Fetoui H, Makni M, Zeghal N, Drira N-E. Phenolic contents and antioxidant activities of date palm (Phoenix dactylifera L.) leaves. International journal of food properties. 2016;15(6):1220-32.
50. Chaira N, Smaali MI, Martinez-Tomé M, Mrabet A, Murcia MA, Ferchichi A. Simple phenolic composition, flavonoid contents and antioxidant capacities in water-methanol extracts of Tunisian common date cultivars (Phoenix dactylifera L.). International journal of food sciences and nutrition. 2019;60(sup7):316-29.
51. Alem C, Ennassir J, Benlyas M, Mbark AN, Zegzouti YF. Phytochemical compositions and antioxidant capacity of three date (Phoenix dactylifera L.) seeds varieties grown in the South East Morocco. Journal of the Saudi Society of Agricultural Sciences. 2017;16(4):350-7.
52. Iranshahi M, Rezaee R, Parhiz H, Roohbakhsh A, Soltani F. Protective effects of flavonoids against microbes and toxins: The cases of hesperidin and hesperetin. Life sciences. 2015;137:125-32.
53. Tang ZX, Shi LE, Aleid SM. Date fruit: chemical composition, nutritional and medicinal values, products. Journal of the Science of Food and Agriculture. 2013;93(10):2351-61.
54. Elleuch M, Besbes S, Roiseux O, Blecker C, Deroanne C, Drira N-E, et al. Date flesh: Chemical composition and characteristics of the dietary fibre. Food chemistry. 2013;111(3):676-82.
55. Saeed HS, Osman B, El-Hadiyah TMH, Mohamed MS, Osman WJ, Abdoon IH, et al. Date palm pollen grains as a potential manager for male sub-fertility: A clinical trial. J Pharm Res Int. 2020;32:83-95.
56. Waly MI. Health benefits and nutritional aspects of date palm pollen. Canadian Journal of Clinical Nutrition. 2020;8(1):1-3.
57. Orabi SH, Shawky SM. Effect of date palm (Phoenix dactylifera) seeds extracts on hematological, biochemical parameters and some fertility indices in male rats. Int J Sci Basic Appl Res. 2014;17(1):137â.
58. Elberry AA, Mufti ST, Al-Maghrabi JA, Abdel-Sattar EA, Ashour OM, Ghareib SA, et al. Anti-inflammatory and antiproliferative activities of date palm pollen (Phoenix dactylifera) on experimentally-induced atypical prostatic hyperplasia in rats. Journal of Inflammation. 2019;8(1):1-13.
59. Orabi SH, Shawky SM. Effect of date palm (Phoenix dactylifera) seeds extracts on hematological, biochemical parameters and some fertility indices in male rats. International Journal of Sciences: Basic and Applied Research. 2014;17(1):137-47.

60. Kordi M, Aghaei Maibodi F, Tara F, Nemati M, Shakeri M. Effect of consumption date fruit on spontaneous labor in primiparous woman. J Obstet Gynecol Infertil. 2013;77:9-15.
61. Al-Kuran O, Al-Mehaisen L, Bawadi H, Beitawi S, Amarin Z. The effect of late pregnancy consumption of date fruit on labour and delivery. Journal of obstetrics and gynaecology. 2016;31(1):29-31.
62. Zhang C-R, Aldosari SA, Vidyasagar PS, Nair KM, Nair MG. Antioxidant and anti-inflammatory assays confirm bioactive compounds in Ajwa date fruit. Journal of agricultural and food chemistry. 2018;61(24):5834-40.
63. Bagherzadeh Karimi A, Elmi A, Mirghafourvand M, Baghervand Navid R. Effects of date fruit (Phoenix dactylifera L.) on labor and delivery outcomes: a systematic review and meta-analysis. BMC pregnancy and childbirth. 2020;20:1-14.
64. Kuswati K, Handayani R. Effect of Dates Consumption On Bleeding, Duration, And Types of Labor. Journal of Midwifery. 2019;4(1):85-91.
65. El-Kashlan AM, Nooh MM, Hassan WA, Rizk SM. Therapeutic potential of date palm pollen for testicular dysfunction induced by thyroid disorders in male rats. PloS one. 2015;10(10):e0139493.
66. Malviya N, Malviya S, Jain S, Vyas S. A review of the potential of medicinal plants in the management and treatment of male sexual dysfunction. Andrologia. 2016;48(8):880-93.
67. Gakunga NJ, Mugisha K, Owiny D, Waako P. Effects of crude aqueous leaf extracts of Citropsis articulata and Mystroxylon aethiopicum on sex hormone levels in male albino rats. International Journal of Pharmaceutical Science Invention. 2014;3(1):5-17.
68. Otify AM, El-Sayed AM, Michel CG, Farag MA. Metabolites profiling of date palm (Phoenix dactylifera L.) commercial by-products (pits and pollen) in relation to its antioxidant effect: A multiplex approach of MS and NMR metabolomics. Metabolomics. 2019;15:1-17.
69. Abedi A, Parviz M, Karimian SM, Rodsari HRS. Aphrodisiac activity of aqueous extract of Phoenix dactylifera pollen in male rats. 2018.
70. Mohamed NA, Ahmed OM, Hozayen WG, Ahmed MA. Ameliorative effects of bee pollen and date palm pollen on the glycemic state and male sexual dysfunctions in streptozotocin-Induced diabetic wistar rats. Biomedicine & Pharmacotherapy. 2018;97:9-18.
71. Elberry AA, Mufti ST, Al-Maghrabi JA, Abdel-Sattar EA, Ashour OM, Ghareib SA, et al. Anti-inflammatory and antiproliferative activities of date palm pollen (Phoenix dactylifera) on experimentally-induced atypical prostatic hyperplasia in rats. Journal of Inflammation. 2011;8(1):1-13.
72. Rasekh A, Jashni HK, Rahmanian K, Jahromi AS. Effect of Palm Pollen on Sperm Parameters of Infertile Man. Pakistan journal of biological sciences: PJBS. 2015;18(4):196-9.
73. Selmani C, Chabane D, Bouguedoura N. Ethnobotanical survey of Phoenix dactylifera L. pollen used for the treatment of infertility problems in Algerian oases. African Journal of Traditional, Complementary and Alternative Medicines. 2017;14(3):175-86.

Review Article

EFFECTIVENESS OF SIMULATION IN NURSING EDUCATION- A NARRATIVE REVIEW OF LITERATURE

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ABSTRACT

Nursing is the fastest-growing career now a days. To be able to work effectively as a nurse after completing training, receiving quality nursing education is the most important factor. Currently, the most effective teaching strategy and method for imparting theoretical knowledge and abilities in the nursing field is simulation. The objective of this literature review is to examine and provide current research on this subject. Literature review was carried out related to the concern derived from Google Scholar, PubMed, CINAHL, ProQuest, Nursing Journal and science direct. It included studies published in English, consuming the following keywords: Simulation, Simulation based education, Nursing, Nursing education. Learning by using simulations allows students to practice in a controlled environment without any fear of harming humanbeings. This will enhance their problem solving skills in clinical practice. Practicing in such protected environment and the sense of safety boost students' self-esteem and self-confidence. This may help in reducing the gap between practice and clinical experience on patients.

Key Words: Simulation, Simulation based education, Nursing, Nursing education

INTRODUCTION

Nursing is the most emerging profession now a days, both the genders including males and females are keenly interested to opt this profession. The essential aspect of becoming a nurse is to get quality nursing education, so that he/she can serve productively after completing their training. Nursing education comprises of two main components including theoretical content and strong command on nursing skills. These are the basic pillars to become a professional nurse. As this profession demands a lot of clinical expertise, which requires lot of hands on practice. Nursing education has flourished with the passage of time. To develop a nurse expertise on the clinical side, simulation based nursing education was introduced. It is one of the artistic way to help nursing students to learn the skills and establish their decision making power on manikins that gives the sense and feeling of a real bedside scenario(1). It has emerged from a single hand for practicing cannulation to high fidelity simulation. It facilitates students to develop clinical expertise by practicing skills on dummy patients. It helps to enrich their communication skills, as a novice student nurse they are very confused about how to introduce themselves to patients or how to handle the critical situations like if the attendants are creating panic(2). This opportunity serves them as a rehearsal ground to polish their skills before they start working on human patients.

The simulation based learning offers to practice in different clinical scenarios, which includes difficult clinical situations as well. In addition, simulation based sessions are carried out under

faculty supervision so that learners can get constructive feedback about their performance. They can make it better according to the guidance of highly trained and skillful mentors. It is also essential to see the efficiency how simulation based learning has made difference in the journey of nursing students. Simulation provides multiple times practice on same skill which is otherwise difficult in real life patient(3). Even with simulators at the beginning, some students feel uncomfortable about learning these skills but after practicing them in the skills lab on manikins they become well confident and learn to become experts with time.

A study by Salma (2020) with the support of pre and post study intervention, a Quasi- experimental study design was conducted to explore the usefulness of simulation based nursing education in teaching end of life care to undergraduate nursing students at a private sector university in Karachi, Pakistan(4). The study participants gave feedback that this study helped them to learn how they have to deal with their emotions, when they are caring for a patient who is near to death. Secondly they have learned to enhance their attitudes and behaviors towards the family and patients who are experiencing these situations. Another study conducted by Carrero (2021) on simulation based education and its effects on nursing students accounts high satisfaction levels among students and they illustrated that their confidence levels have raised by this teaching pedagogy(5). It is evident from the above studies that teaching simulation based education, facilitates students in gaining best skills to serve the patients. A strong literature review is carried out to find out the effectiveness of simulation based nursing education introduced for the students.

As it is evident from the above mentioned studies that, it is very effective strategy to utilize simulation based nursing education for nursing students. It is essential to identify strategies to help students learn through this teaching modelity and to make ways to use these facilities at its best. Therefore, the purpose of this review was to explore the level of knowledge and confidence development by the use of simulation based education for nursing students, to check the attitude and behavioral changes of students that they develop through simulation based education and to examine the development of effective communication skills and to find the strategies to make this more acquainted and beneficial for students.

METHODS

Search Strategy

Literature search was done using Google Scholar, PubMed, CINAHL, ProQuest, Nursing Journal and science direct. “Simulation based nursing education, Strategies proposed to effectively utilize simulation based education, effectiveness of simulation based education, simulation based nursing education benefits for student nurses, knowledge enhancement of nursing students by simulation, faculty perception on simulation based education, high fidelity simulation and nursing student’s perceptions”, were used as keywords in searching articles. Total number of articles searched were 33 which included articles from various fields after sorting out for nursing linked articles 20 were selected, out of which 11 were offered as full text articles and when the abstracts were screened for most relevant and suitable articles, 07 were finally identified. Literature on simulation based nursing education in Pakistani (local) context was also searched and only one article was identified. A summary of the literature search is given in Figure 1.

LITERATURE ANALYSIS

With the advancement in time and technology, health related domains are also showing great progression. Nursing being the fundamental part of the healthcare system has also evolved with passage of time. This has involved advanced teaching methodologies, well qualified trainers, producing trained and skilled nurses. Simulation based education plays a vital role in preparing

practically equipped nurses. A skills oriented pedagogy, used to teach nursing care to the students. It is a teaching methodology through which the gap between theoretical knowledge and practical application can potentially be filled(6).

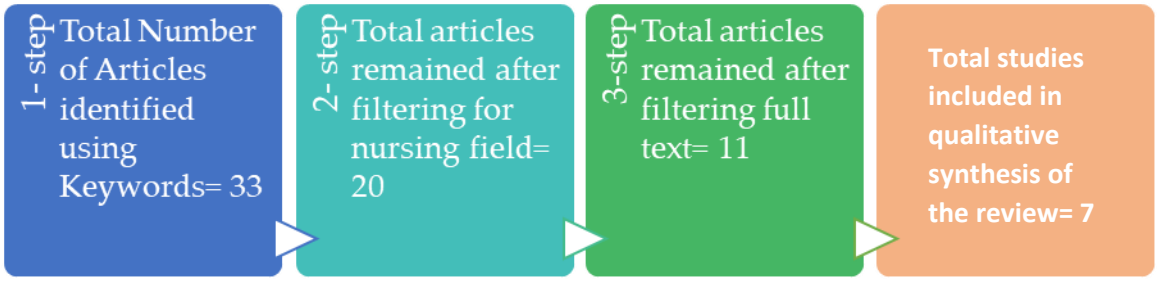

Figure 1. Summary of the literature review – screening, identification and selection of studies

Simulation based education prepare nursing students in various ways. This teaching method helped the students to gain a lot of knowledge and confidence through practicing skills in a specified area where manikins are present. When students get a chance to practice skills on manikins, it benefits them to develop more knowledge and understanding, as they are performing different scenarios including critical incidents so they get a chance to learn how to deal with them in actual setup. To practice it more thoroughly they can even repeat it multiple times to polish their skills and get perfect hands-on, so that they get well prepared to apply it on real patients.

When students perform skills on dummy's they gain confidence because as a student it is difficult to directly perform on the actual patients. They are novice so they become very anxious but with repetitive practice they get comfortable and competent. According to a research study this method facilitates students to manage their anxiety and fear related to dealing with patients in real bedside experiences. This helps them to practice in safe boundaries where there is no chance of harm(5).

Another domain in which simulation based education has worked is the attitude and behavioral modification. As student nurses the transition from didactic teaching to functioning as student nurse in clinical setup is very difficult, as they are not aware of the actual situation of bedside setup. This approach provides exposure on how to deal with those situations that are emotional or sensitive. It gives experience and makes a nurse stronger to deal with the critical conditions.

According to the research study high fidelity simulation facilitated nursing students to deal with patients who are at the end of their life's. It is the most crucial stage in the clinical experience. It is very important that the nurse should be proficient to handle these sort of panic circumstances. Simulation based practices helped nursing students to learn how to control their feelings and emotions while having these sort of situations. It facilitated them to get relaxed from the fear of unfamiliar scenarios. The most essential goal that is achieved through this practice is the accomplishment of quality care outcomes(4). When the author was serving as a student nurse and was assigned in the oncology unit, she encountered a scenario where an 18year old boy was suffering from lung cancer. He was extremely sick, on continuous bipap support. The family was very concerned; all the members of the family were literally crying as the patient was very young and was fighting the battle of life and death. The author was also crying while standing at a side, unable to hold emotions. Thus simulation based approach would have helped students as well if they have practiced such scenarios in the lab. Because a nurse should be the strong person to deal with these sort of circumstances. If a nurse start crying and feeling down, then who would be the

one to take care of this situation. This approach is the best one to teach nurses about their behavioral and attitude adaptation. One more aspect that is well established through simulation based teaching pedagogy is communication skills. It is the most important feature of a professional nurse that, they must use effective communication techniques including verbal and non-verbal cues to deliver something to the patients and their families. If the communication is effective and therapeutic then a nurse can efficiently deal with any sort of situations. Either it is a normal meet and greet or a critical panic state. But, when we talk about nursing students, they are very new to the profession. They don't know how to dialogue with the patients and their families? How to explain medical terminologies? How to talk when there is a code blue or life threatening situation? They must be skilled to deal all this. Thus, simulation based approach is the best platform where they can learn how to handle them with effective and therapeutic communication techniques. Through this they can identify their flaws and again they can practice it more to gain self-confidence. According to a study, simulation based clinical practices enables nursing students to enhance and nurture their communication skills and polish their cognitive abilities to perform more productively in the patient care areas(7). This teaching pedagogy can be made more fruitful for the nursing students by providing high fidelity simulation arrangements in which they can learn with advance technology. Secondly, nursing faculty should be competent and qualified to conduct simulation sessions. They must be well acquainted to the advance manikins. Thirdly, there should be a system of providing feedback to the students while they are performing, so they can improve their skills and can apply them in their clinical rotations and further more in their professional life.

CONCLUSION

Simulation based teaching is hence an effective and advantageous pedagogy for teaching nursing students to enrich their skills and give best patient outcomes in their clinical experience. Students have found a drastic change in their teaching and learning journey, when they were introduced with this effective method to polish themselves. It should be used in all the setups to help students develop their skills and empower their knowledge to achieve quality care which is the chief goal of nursing profession.

REFERENCES

1. Kim J, Park J-H, Shin S. Effectiveness of simulation-based nursing education depending on fidelity: a meta-analysis. BMC Med Educ. 2016 Dec 23;16(1):152.
2. Aebersold M. Simulation-Based Learning: No Longer a Novelty in Undergraduate Education. OJIN Online J Issues Nurs. 2018 Apr 3;23(2).
3. Shin S, Park J-H, Kim J-H. Effectiveness of patient simulation in nursing education: Meta-analysis. Nurse Educ Today. 2015 Jan;35(1):176–82.
4. Rattani S, Kurji Z, Khowaja A, Dias J, AliSher A. Effectiveness of high-fidelity simulation in nursing education for end-of-life care: A quasi-experimental design. Indian J Palliat Care. 2020;26(3):312.
5. Carrero-Planells A, Pol-Castañeda S, Alamillos-Guardiola MC, Prieto-Alomar A, Tomás-Sánchez M, Moreno-Mulet C. Students and teachers' satisfaction and perspectives on high-fidelity simulation for learning fundamental nursing procedures: A mixed-method study. Nurse Educ Today. 2021 Sep;104:104981.
6. Eyikara E, Baykara ZG. The importance of simulation in nursing education. World J Educ Technol Curr Issues. 2017 Jan 2;9(1):02–7.
7. Luo D, Yang B-X, Liu Q, Xu A, Fang Y, Wang A, et al. Nurse educators perceptions of simulation teaching in Chinese context: benefits and barriers. PeerJ. 2021 Jun 17;9:e11519.

Case Report

POST-TUBERCULOUS MENINGITIS HYDROCEPHALOUS- A CASE REPORT

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ABSTRACT

Mycobacterium tuberculous bacteria infect host lungs while inhaling them from the external environment, causing a localized infection with a potential to spread to local lymph nodes. The bacilli have the property to disseminate to other organs including Central Nervous System (CNS) and lead to tuberculous meningitis (TBM). The bacilli may develop tiny sub-pial or sub-ependymal rich foci. These rich foci get larger as the illness worsens and may finally burst into the sub-arachnoid region, causing meningitis. Tuberculous meningitis is linked to a high mortality rate. The majority of TBM patients who survive have long term neurological disabilities. This case was presented to Aga Khan University Hospital Karachi, Pakistan and the patient has taken Leave Against Medical Advice twice due to financial crises.

Key Words: Hydrocephalus, Tuberculous meningitis, Mycobacterium

INTRODUCTION

Mycobacterium Tuberculosis bacteria infect host lungs while inhaling them from the external environment, causing a localized infection that radially spreads to local lymph nodes. The bacilli have the property to disseminate to other organs including Central Nervous System(CNS) and lead to tuberculous meningitis (TBM). The bacilli may develop tiny sub-pial or sub-ependymal rich foci. These rich foci get larger as the illness worsens and may finally burst into the sub-arachnoid region, causing meningitis (1) .

Tuberculous meningitis is linked to a high mortality rate. The majority of TBM patients who survive have debilitating neurological consequences. One of the frequent complications of TBM, which affects a considerable number of patients, is hydrocephalus. The development of hydrocephalus may occur paradoxically following the start of anti-tuberculosis therapy or it may be a presenting symptom. A thick, gelatinous exudate, which is predominately present in the basal portions of the brain, is the defining pathological trait of TBM. Cranial nerve trunks like the optic nerve, optic chiasma, and arteries of the circle of Willis are encased and strangulated by exudate. The cerebrospinal fluid (CSF) flow to the brain is also obstructed by basal exudate, which causes ventriculomegaly. In order to differentiate between the two common types of hydrocephalus i.e. communicating and obstructive on the basis of routine neuroimaging Computed Tomography (CT) scan and Magnetic Resonance Imaging (MRI) are done(2).

Presentation:

A middle age female patient with, a known case of Hypertension(HTN) and TBM, came to the emergency(ER) department with complaints of headache for 3 weeks, high-grade fever, and gradual

vision loss for one and a half months. No history of loss of consciousness or seizures. MRI was done at Nawab Shah Civil Hospital, which showed non-communicating Hydrocephalus and Ventriculitis for which she was taken to Zia Uddin Hospital. In Zia Uddin Hospital management of the patient started with the given diagnostic procedures; lumber puncture was done; which showed some abnormalities. The patient took Leaving Against Medical Advice (LAMA) and arrived at Aga Khan University Hospital(AKUH) Emergency department on 1st Nov 2022. On arrival at AKUH, the patient's Glasgow Coma Scale (GCS) was 7/15 for which she was immediately intubated, an urgent CT scan was done which showed a space occupying lesion in the left frontal lobe causing acute obstructive hydrocephalus. She was rushed to operation room for endoscopic septum Pellucidotomy + left External Ventricular Drain insertion and then shifted to Intensive care unit (ICU) for postoperative critical care.

Diagnostic Criteria:

Due to a lack of quick, reliable diagnostic testing, tuberculous meningitis diagnosis is often delayed, which negatively impacts the prognosis. The most extensively used and straightforward diagnostic test for diagnosing tuberculous meningitis is ziehl-neelsen staining, but its sensitivity varies significantly by region(3).

A brain biopsy is a procedure to extract an aberrant tissue sample for microscopic analysis. If an abnormality is detected on an MRI or CT scan, the tissue cells removed during the biopsy can reveal what kind of abnormality is present. There is significant pleocytosis with an increasing amount of lymphocytes, increase CSF protein level, and a marked reduction in CSF glucose levels (hypoglycorrhachia) in typical TBM(4). CT scanning and MRI are both utilized in the TBM to diagnose hydrocephalus. The preferred imaging method is a contrast CT scan, which revealed a space-occupying lesion in the left frontal lobe causing acute obstructive hydrocephalus. This gives us a piece of adequate information on subependymal seepage, the size of the ventricles, the presence of tuberculomas, and cerebral edema(2).

Differential Diagnosis and Current Diagnosis

Tuberculous Meningitis can be doubted with many differential diagnoses like; Encephalitis, Carcinomas, Stroke, Cerebral aneurysm, Collagen vascular disease, and lupus. The final medical diagnosis of our patient was post-TBM hydrocephalous because hydrocephalous is one of the most found one problems of TBM and is shown by literature that 80 percent of TBM patients develop Hydrocephalous as a complication(2).

Non-Pharmacological Interventions

Two Surgical interventions were performed on this patient as per clinical indication:

1. Endoscopic septum Pellucidotomy
2. External Ventricular Drain (EVD) Placement

The septum pellucidum is a thin, bilateral membrane tissue that serves as the boundary between the lateral ventricles, an often utilized procedure for the surgical treatment of unilateral hydrocephalus is Endoscopic septum Pellucidotomy(5).

The most frequent and crucial life-saving procedure in a surgical intensive care unit is the placement of an EVD, which enables the removal of cerebral spinal fluid from the ventricles and into a sealed external environment. The regular intracranial pressure monitoring and CSF deviation offered by an EVD are beneficial for treating various acute brain injuries(6).

Table 1. Summary of the pharmacological management of the patient

Medication	Indication	Dosage and Frequency
Inj. Levetiracetam	Prevent seizures associated with hydrocephalus	500mg Twice a day
Tab. Pyridoxine	To prevent the development of peripheral neuropathy	50mg Once a day
Inj. Dexamethasone	They are believed to lessen pressure inside the brain, which in turn lowers the chance of mortality by reducing inflammation of the surface of the brain and accompanying blood vessels.	6mg Twice a day
Inj. Vancomycin	Glycopeptide antibiotics	750mg Twice a day
Inj. Meropenem	β-lactam antibiotic for infection	2000mg Twice a day
Tab. Omeprazole	Indigestion, heartburn	40mg Once a day
Tab. Surbex Z	Vitamin B-Complex, Vitamin C, and zinc deficiencies.	1 tablet Once a day
Inj. Tramadol	For pain	25mg As needed

In this patient interval placement of ventricular drain with improvement in cystic dilatation present along the left lateral ventricles. Grossly unchanged edema along occipital and lateral ventricles with dilated temporal horns. There is re-demonstration of unchanged size of ventricles. Interval resolution of previously noted speck of air with re-demonstration of hemorrhage along the track of ventricular drain. The bi-frontal diameter currently measures 28.4 mm and previously measured 28.7 mm, showing no significant interval change.

DISCUSSION

According to world health organization (WHO) each year 10.4 million cases of tuberculosis occur and of which the dissemination to central nervous system is 1 lakh in the form of Tuberculous meningitis(7). A review in Iran was done which shows that each year the cases of extra pulmonary TB are increasing day by day and 1651 cases were diagnosed of TBM in between the years of 2000 to 2021 only in Iran. Sistan, Baluchestan, South Khorasan, and Mazandaran had greater rates of TB meningitis than other provinces. Fever, anorexia, headache, stiff neck, loss of consciousness, and vomiting were the most typical signs of tuberculous meningitis(1). The frequent complication of TBM is hydrocephalus, which can occur in up to 85% of affected children. Children experience it more severely than adults do. There are two types of Hydrocephalous the communicating and the obstructive(8).

Critical Points for Reflection

Due to the two times LAMA, this case was very unusual. The patient took LAMA once while aiming for a favorable prognosis and again because of a financial crisis. Due to poor adherence to the anti tuberculosis therapy (ATT) medications, our patient developed hydrocephalous post-tuberculous meningitis. Good ATT compliance is necessary to ward off miliary TB. Also, financial difficulties shouldn't affect the patient's prognosis. We tracked down the patient using our contacts, and the patient was successfully discharged.

REFERENCES

1. Mortazavi-Moghaddam S, Pagheh A, Ahmadpour E, Barac A, Ebrahimzadeh A. Tuberculous meningitis and miliary tuberculosis in Iran: A review. Asian Pac J Trop Med. 2022;15(4):143.
2. Paliwal V, Garg R. Hydrocephalus in Tuberculous Meningitis - Pearls and Nuances. Neurol India. 2021;69(8):330.
3. Zou Y, Bu H, Guo L, Liu Y, He J, Feng X. Staining with two observational methods for the diagnosis of tuberculous meningitis. Exp Ther Med. 2016 Dec;12(6):3934–40.
4. Shirani K, Talaei Z, Yaran M, Ataei B, Mehrabi-Koushki A, Khorvash F. Diagnosed tuberculous meningitis using cerebrospinal fluid polymerase chain reaction in patients hospitalized with the diagnosis of meningitis in referral hospitals in Isfahan. J Res Med Sci. 2015 Mar;20(3):224–7.
5. Barany L, Meszaros C, Ganslandt O, Buchfelder M, Kurucz P. Neural and vascular architecture of the septum pellucidum: an anatomical study and considerations for safe endoscopic septum pellucidotomy. J Neurosurg . 2020 Sep;133(3):902–11.
6. Muralidharan R. External ventricular drains: Management and complications. Surg Neurol Int. 2015;6(7):271.
7. Seddon JA, Tugume L, Solomons R, Prasad K, Bahr NC. The current global situation for tuberculous meningitis: epidemiology, diagnostics, treatment and outcomes. Wellcome Open Res. 2019 Nov 5;4:167.
8. Rajshekhar V. Management of hydrocephalus in patients with tuberculous meningitis. Neurol India. 2009;57(4):368.

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