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Cook NR, Rosner BA, Hankinson SE, Colditz GA. Mammographic screening and risk factors for breast cancer. American Journal of Epidemiology. 2009 Dec;170(11):1422-32. doi: 10.1093/aje/kwp304.

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ACKNOWLEDGEMENT

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TABLE OF CONTENTS

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Volume 4, Issue 8 (August 2023)

Medical Research Ethics and Integrity in Pakistan: Ensuring Rigorous and Responsible Research Practices

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Medical research stands as a cornerstone of progress in healthcare, yielding insights that drive advancements in diagnosis, treatment, and patient care. In Pakistan, a country with a rapidly evolving healthcare landscape, the significance of upholding impeccable research ethics and integrity cannot be overstated. Ethical considerations are not mere formalities; they are the bedrock on which reliable and credible research rests. Striving for scientific excellence demands a commitment to transparency, honesty, and adherence to ethical principles at every stage of research. The pursuit of robust research ethics encompasses several key dimensions. Foremost among these is the protection of human subjects. The ethical responsibility to ensure the well-being, rights, and informed consent of participants cannot be compromised. Equally vital is the need to safeguard the credibility of research findings. Fabrication, falsification, and selective reporting erode the very foundation of scientific inquiry and trust. In this regard, fostering a culture of accountability, where researchers are held to high standards of integrity, is imperative. Pakistan's research institutions must provide clear guidelines and promote educational programs that empower researchers to navigate complex ethical dilemmas. As Pakistan's healthcare system becomes more interconnected with the global scientific community, harmonizing ethical standards is of paramount importance. International collaborations demand mutual respect for research ethics and data integrity. However, to achieve this, Pakistan must continue strengthening its regulatory framework and research oversight mechanisms. Regulatory bodies play a pivotal role in ensuring compliance with ethical guidelines and in investigating allegations of misconduct. By bolstering these mechanisms, Pakistan can inspire confidence in the quality and credibility of its research endeavors. In conclusion, upholding medical research ethics and integrity in Pakistan is not a mere formality but a pledge to scientific rigor and societal well-being. The research community, regulatory bodies, and educational institutions must unite to foster a culture where ethical considerations are central to every research endeavor. Through unwavering commitment to rigorous and responsible research practices, Pakistan can both contribute meaningfully to the global body of knowledge and elevate its healthcare system for the benefit of its citizens.

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Review Article

Novel Approaches for Treatment of Epilepsy

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ABSTRACT

Epilepsy is a serious neurological disorder on the juncture of psychiatry and neurology. It is characterized by recurrent and episodic seizures which are due to excessive discharge by the brain neurons. The therapeutic response failure of more than one or two antiepileptic drugs (AEDs) is the benchmark of refractory or intractable epilepsy. The aim of the study was to determine new approaches which lead towards the treatment of epilepsy. In order to treat focal mesial temporal lobe epilepsy or neocortical epilepsy in adults and any malformation of cortical development such as focal dysplasia surgical resection remains the gold standard treatment. Disconnection procedures such as corpus callostomy and multiple subpial transections are the best alternative treatment for that patient whose seizure origin is in eloquent cortex or having generalized epilepsy syndromes. Palliative neuromodulation procedures such as Vagus nerve stimulation (VNS), Responsive neurostimulation (RNS) and Deep brain stimulation (DBS) are best approach to treat intractable epileptic patients who are not suitable candidates of surgery. As the search of better management of epilepsy continues gene therapy and optogenetics gain a momentum in neuroscience.

INTRODUCTION

Epilepsy is one of the neurologic disorders that is characterized by recurrent episodic seizures. It can occur at all ages due to different causes [1]. In developed countries the incidence rate of epilepsy is 50 per 100,000 and prevalence rate is 5 to 10 per 1000. However, up to 30% people with epilepsy remain resistant to treatment despite treatment with monotherapy and polytherapy of antiepileptic drugs (AED). Time and countless effort have been invested by researchers to develop better treatment approaches such as antiepileptic devices, nano particles for targeting epileptic focus and gene therapy [2, 3]. There are five theories which explain the causes of thermoresistant epilepsy such as, transporter hypothesis, target hypothesis, gene variant hypothesis and the intrinsic severity hypothesis. The normal human brain is protected by P glycoprotein(P-gp), multi drug resistance gene 1(MDR1), which is found only in the vicinity of blood vessels on endothelial cell membrane that constitute BBB and multi drug resistance associate's protein 1 (MRP1), which is found only in the choroid plexus epithelium. Normally, P-glycoprotein(P-gp) export the drug out of cell in order to protect the cells against influx of xenobiotics. P-gp transport few AEDs, several AEDs have similar chemical structure to P-gp substrate [4, 5]. Hence it can be concluded that the inhibition of P-glycoprotein may contribute towards the treatment of patients suffering

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from antiepileptic drug resistant epilepsy [6]. Hence, researchers are of the view that the genetic variation of the genes encoding enzymes that are responsible for metabolism of antiepileptic drugs, drug receptors and ion channels may be responsible for the resistance faced by some individuals in case of antiepileptic drug therapy [7, 8]. As shown in Figure 1, there are various novel treatment approaches for treating epilepsy. This study provides an extensive review of various novel treatment approaches (Figure 1) that have been used for the treatment of the epilepsy.

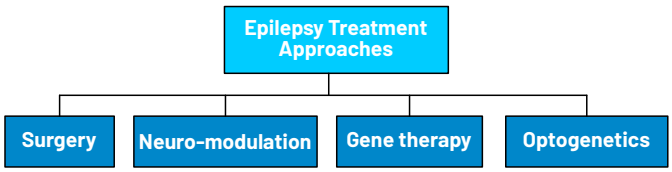

Figure 1: Various treatment approaches for epilepsy

SURGERY

Current AEDs which mainly targets ion channels and transmitter receptors are only effective in 60-70% of individuals idiopathic generalized epilepsy can be easily controlled by medication than the focal epilepsies and symptomatic generalized epilepsies [9, 10]. Epilepsy surgery can be divided into two categories, resective and disconnective procedures. The former includes lesionectomy, corticectomy, and lobectomy. The latter comprises MST (multiple subpial transections), corpus callosotomy, and hemispherotomy [11]. Surgical intervention need not be considered only as a last resort [12].

HEMISPHRECTOMY

The best candidates for hemisphrectomy are patients having progressive (Rasmussen's encephalitis and Sturge-Weber syndrome), acquired (e.g.; intracranial hemorrhage, hemiconvulsion-hemiplegia-epilepsy syndrome, and other sequelae of brain trauma and infection) developmental (e.g., cortical dysplasia, hemimegalencephaly) etiologies [13, 14]. Depending upon etiology and extension of anatomic abnormality there are three different surgical techniques.

Anatomic hemispherectomy

In anatomic hemisphrectomy lobes such as temporal, frontal, parietal and occipital lobes are removed with the preservation of the basal ganglia, insular cortex and thalamus.

Functional hemispherectomy

In functional hemispherectomy the procedures which are performed are (a) temporal lobectomy which extend to the trigone including hippocampus amygdala, (b) central excision in which lateral ventricle is exposed, (c) disconnection of corpus callosum from the ventricle to the course of anterior cerebral artery and pericallosal to the basal frontal region, and (d) posteriorly, corpus callosum is followed by subpial disconnection through temporal lobectomy to perform mesial parietooccipital disconnection.

Modified anatomic hemispherectomy

Modified anatomic hemispherectomy is similar to anatomic hemispherectomy but in modified anatomic hemispherectomy the disconnection of frontal or occipital lobes or both are preserved depending upon the etiology, anatomic abnormality and the location of epileptogenic zone. This progression began with the development of hemidecortication and functional hemisphrectomy in the 1970's and 1980's. further in 1990s several different approaches such as hemispherotomy was introduced [15-17].

Corpus Callostomy

Corpus Callostomy is a palliative surgical procedure which is performed in those patients who suffer from idiopathic generalized epilepsy (IGE) and are not the best suitable candidates of focal resection [18]. Seizures in IGE occur due to the absence of structural lesions or are inherited in nature [19]. Approximately in 40% to >70% of patient's seizure frequency and severity may reduce [20, 21]. In corpus callostomy complete section corpus callosum, anterior two third or three-fourth callostomy or anterior and posterior callostomy is performed. At present the most common procedure is two-third callostomy because of the less complications as compared to complete callostomy.

Multiple Subpial Transections (MST)

MST is one of the most novel approaches which are extensively used in those patients in which epileptogenic zone cannot be resected because it lies in eloquent cortex. In this method the horizontal connections which lies between the cortical neurons and are responsible for the propagation of the epileptic discharges is sectioned in this procedure [22]. MST can be performed alone or in combination with resective surgery such as a lesionectomy or large disconnections to treat epileptogenic foci present in eloquent cortex. MST not only treat unifocal epilepsy but also effective to treat Landau-Klefener Syndrome (LKS) in children and multifocal epilepsy in adults [23]. Hence, it was concluded that MST proved to be an alternative treatment for RSE [24].

NEUROMODULATION

Neuromodulation has become a major field of innovation in epilepsy therapy. Neuromodulation are palliative procedures which are minimal invasive and non-respective. In neuromodulation electrical pulses are directly administered to nervous tissue to stimulate a pathologic substrate in order to achieve a therapeutic effect (Figure 2). There are three neuromodulation

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techniques. Hence in case of such patient's neuromodulation is utilized [25].

VNS

Vagus nerve stimulation (VNS) as shown in Figure 2, is a neuromodulatory technique that stimulates the left vagus nerve [26]. Other than epilepsy, VNS is also use for mood improvements and for the treatment of drug resistant depression [27] hence VNS become a feasible treatment option in both neurology and psychiatry [28]. In worldwide more than 100,000 VNS devices were implanted in more than 75000 patients in August, 2014 [29]. In VNS battery-powered device which looks similar to cardiac pacemaker is implanted in the upper chest and electrodes with 2 connecting wires are placed subcutaneously to the left vagus nerve. The generator is connected by a wand and is attached with a laptop for monitoring. VNS is a broad-spectrum treatment and is very effective in refractory focal onset seizure patients. It can be used in those patients who already had surgical treatment.

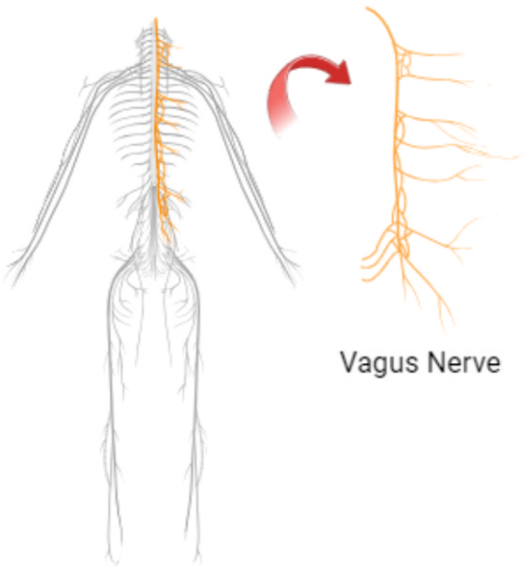

Figure 2: Vagus Nerve Stimulator

DBS

Deep brain stimulation (DBS) is one of the open loop systems. In DBS the target sites for stimulation are anterior nucleus of thalamus, centromedian thalamus, thalamus and seizure focus [30, 31]. Anterior nucleus deep brain stimulation (AN-DBS) was reported by copper and Upton for the first time. AN-DBS was introduced by these researchers for the treatment of complex partial seizures. The main idea behind this approach was the data collected over the year about the involvement of AN in the occurrence of generalized seizures [32]. Furthermore, it was concluded after research on animal-based models that high- frequency stimulation of AH may result in the increased seizure threshold or reduction in the frequency of seizures or both [33-35].

RNS

RNS is a closed loop stimulation which have an ability to stimulate the seizure focus automatically after the spontaneous detection of seizures. In this technique depth and subdural electrodes along with the neurostimulator is implanted in the cranium where seizure focus is located. According to a study performed by a group of researchers in 2011 concluded that there was a seizure reduction in intractable partial epileptic patients by receiving RNS [36]. RNS received FDA approval for the treatment of partial onset epilepsy in adults, in 2013 [25].

GENE THERAPY

In the past two decades advancement in technology and genetics led the researchers towards the discovery of almost 1000 genes solely associated with epilepsy [37]. Therefore, gene therapy (Figure 3) techniques can be used as an alternative to respective surgeries in case of patients suffering from intractable focal epilepsies. The main idea behind the gene therapy approaches is the transfer of therapeutic genes into the ictogenic areas of the brain. These therapeutic genes are involved in the expression of neuromodulatory molecules having special anticonvulsive and antiepileptic properties [38, 39].

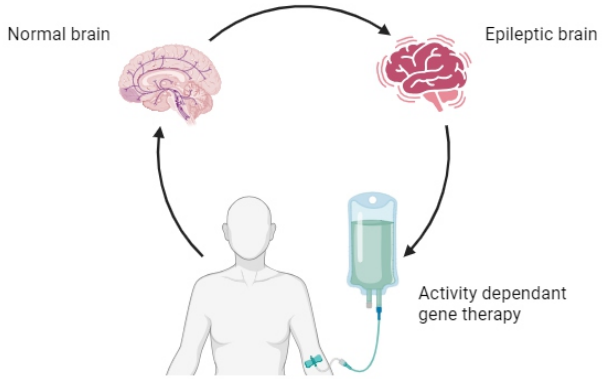

Figure 3: Gene Therapy

Neuropeptide System in Gene Therapy

Galanin in Gene Therapy

A12 neuropeptide system known as galanin system is most abundantly expressed in the temporal lobe of the brain. This system releases galanin which is a neuro peptide. Galanin acts by suppressing the excitatory glutamatergic neuronal transmissions which are involved in seizures [40]. Researchers developed viral vectors which act by exogenously releasing galanin in order to suppress the seizures. This approach was one of the first therapeutic approaches which are used to suppress seizures by the help of gene therapy [41].

NPY Gene Therapy

Neuropeptide Y (NPY) system is another neuropeptide

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system that is widely expressed in the brain. NPY naturally released in the brain by NPY system plays a vital role in controlling seizures [42]. Hence NPY is considered as a target candidate in case of antiepileptic gene therapy approach. Researchers are developing NPY gene therapy which will soon be entering the clinical trials for specifically treating temporal lobe epilepsy. This approach would prevent the surgical removal of ictogenic tissues [43].

OPTOGENETICS

Optogenetics is an evolution in the treatment of neurological disorders. It's a new advanced technique for the treatment of intractable epilepsy. Optogenetics is a combination of optical technology and gene targeting of neurons or proteins. If patients are not suitable candidates for surgery, then they are subjected to neuro stimulation such as VNS for the reduction of the seizure frequency. But if patients are suffering from post-surgical relapse, remission [44] or bilateral temporal lobe epilepsy or having seizure focus in eloquent cortex then they can get benefit from such an advanced and fascinating molecular-genetic tool which is known as Optogenetics. In this technique light sensitive proteins which are known as opsins are used [45, 46] which manipulate the brain activity. This fascinating approach can be used to treat epilepsy [47].

OTHER TREATMENTS OF EPILEPSY

Some other previous treatments used for treating epilepsy are mentioned in Table 1.

Table 1: Other Treatments of Epilepsy

Treatment Approaches	Interventions Used	Main Uses	References
Pharmaceutical approaches	Carbamazepine	Decrease nerve impulses that are responsible for causing seizures.	[48]
	Lamotrigine	Used as a first- line drug for generalized and focal seizures.	[49]
	Zonisamide	Used for generalized and focal seizures.	[48]
	Gabapentin	Used for generalized and focal seizures.	[48]
Therapeutic approaches	Cognitive Behavioural therapy	Restructuring of maladaptive thought patterns.	[50]
	Progressive muscle relaxation	Tense a group of muscles while breathing in and relaxes them while breathing out.	[51]
	Yoga	Release tension in key joints through combination of body postures.	[52]
Natural approaches	Herbal treatments	Found to be involved in potentiation of GABAergic activity in brain.	[53]
	Ketogenic diet	Neurotransmitter modulation in brain by ketone bodies.	[54]
	Vitamin D3	Increase Ca2+ uptake and decrease neuronal excitability.	[55]

CONCLUSIONS

There are many approaches to treat epilepsy. Among all approaches surgical treatment remain the gold standard to treat temporal lobe epilepsy, any malformation in cortical development or to treat any lesion. Alternative treatments for those patients who are not suitable candidates for resective surgery is neuromodulation. There are three types of neuro modulation and all of them are safe and effective in terms of reducing frequency of seizures. The best candidates for RNS and DBS are those patients whose seizure origin is in eloquent cortex. Optogenetics proved to be very effective in animal models to reduce the frequency of seizure. However, still some research such as optimization of light delivery, opsin introduction is required to be done before its application in humans.

Authors Contribution

Conceptualization: MAW, MS, MF

Writing-review and editing: MAW, MS, MF, TM, MSN, NT, DI, MR, AQ, MW

All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

The authors declare no conflict of interest.

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Original Article

Sonographic Changes in Endometrium after Use of Tamoxifen in Breast Cancer

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ABSTRACT

Breast cancer poses a significant global health concern affecting a large number of women. Treatment strategies for breast cancer often involve the use of hormonal therapy, such as tamoxifen. However, the use of tamoxifen is associated with potential side effects, particularly in the endometrium. **Objective:** To evaluate the sonographic changes in the endometrium following the use of tamoxifen therapy in breast cancer patients. **Methods:** It was a quasi-experimental trial conducted at the Department of medical oncology, Jinnah Postgraduate Medical Center, Karachi, Pakistan from Jan 2023 to Jun 2023. Patients aged 18 years or older, histologically confirmed hormone receptor-positive breast cancer, and having tamoxifen treatment with a dose of 20mg/day for at least six months were included. Endometrial evaluation using transvaginal ultrasonography performed by experienced sonographer and sonographic parameters were assessed. Endometrial evaluation was conducted at baseline and 6 months after start of tamoxifen at regular interval as determined by the treating physician. **Results:** The median duration of tamoxifen therapy was 24 months with IQR as 10 to 36 months. There was statistically significant difference in pre-treatment and post-treatment endometrial thickness with p-value=0.0001. About 80.5% of the females had endometrial thickness difference of less and equal to 5mm and polyps were observed in 5 cases. **Conclusions:** Tamoxifen increases the risk of endometrial abnormality; this study highlights the need for monitoring endometrial changes before and after starting tamoxifen therapy in breast cancer patients to detect early suspected neoplastic changes in endometrium.

INTRODUCTION

Breast cancer poses a significant global health concern affecting a large number of women [1]. Treatment strategies for breast cancer often involve the use of hormonal therapy, such as tamoxifen (TMF), to target hormone receptor-positive tumors [2]. TMF, a selective estrogen receptor modulator (SERM), is frequently prescribed as an adjuvant therapy for breast cancer patients, which leads to improved survival rates, reduces mortality rate and decreased risk of recurrence [2, 3]. However, the use of tamoxifen is associated with potential side effects, particularly in the endometrium [4]. Tamoxifen is a selective ER modulator. It has an antagonistic effect on the ER-α receptors in breast tissues and an agonistic effect on the ER- β receptors in the endometrial tissues. This agonistic effect has been shown to increase the rate of several benign and malignant endometrial pathologies such as hyperplasia, atypia, carcinomas, and sarcomas [5, 6]. These concerns have prompted the need for monitoring the endometrial changes induced by TMF to ensure early detection and appropriate management of any abnormalities [4-6]. Transvaginal ultrasound (TVUS) has emerged as a valuable

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non-invasive imaging modality to assess the endometrium and detect tamoxifen-induced changes. TVUS provides a high-resolution image of the endometrium, enabling the evaluation of parameters like endometrial thickness, echogenicity, and morphological characteristics [7, 8] This imaging technique has become a routine practice in monitoring endometrial changes in breast cancer patients receiving tamoxifen therapy [7-9]. Early detection of TMF-induced changes in the endometrium can facilitate timely intervention and management, reducing the risk of developing endometrial pathologies. Sonographic assessment of the endometrium provides a non-invasive, easily accessible, and cost-effective method to monitor these changes throughout the course of TMF therapy. However, limited studies in Pakistan are available to assess the sonographic changes in the endometrium following the use of TMF in breast cancer patients. So, the aim of current study was to see sonographic changes in endometrium by tamoxifen in our population, by assessing endometrial thickness, morphology, and other relevant parameters using transvaginal ultrasound, we aim to provide further insights into the impact of TMF on the endometrium and contribute to the development of effective monitoring strategies in our population.

METHODS

It was a Quasi-Experimental trial conducted at the Department of Medical Oncology, Jinnah Postgraduate Medical Center, Karachi, Pakistan from Jan 2023 to Jun 2023. Sample size of 154 was estimated using Open epi sample size calculator by taking statistics of endometrial hyperplasia as 16.3% among post-menopausal females with breast cancer after Tmf use [10], margin of error as 5% and 95% confidence level. Inclusion criteria was consisted of patients aged 18 years or older, histologically confirmed hormone receptor-positive breast cancer, and having tamoxifen treatment for at least six months. Females having pre-existing endometrial pathology (benign or malignant) or severe renal or liver impairment or pregnancy or Venous thrombo embolism or breast-feeding mothers was excluded from the study. Non-probability consecutive sampling technique was applied for sample selection. The study protocol was reviewed and approved by the institutional ethics committee, ensuring the protection of patients' rights, confidentiality, and informed consent. Verbal informed consent was obtained from all the patients. Demographic and clinical data were collected from all the patients, including age, body mass index (BMI), parity, gravida, family history of breast cancer, menopausal status, and duration of TMF therapy. All non-metastatic ER/PR +ve patients were treated with tamoxifen 20mg/day. Transvaginal ultrasound was performed by experienced sonographers using high-resolution ultrasound machines. Sonographic measurements were conducted at baseline (prior to tamoxifen initiation) and 6 months after start of tamoxifen therapy, as determined by the treating physician. Here we consider an endometrial thickness of ≥ 12 mm as thickened endometrium in an asymptomatic premenopausal woman with regular menses. For postmenopausal and amenorrheic premenopausal women, an endometrial thickness ≥5 mm was defined as endometrial thickening. Endometrial biopsy was indicated if the patient has thickened endometrium, abnormal TVS u/s, or abnormal uterine bleeding. Sonographic parameters including endometrial thickness, the presence of any focal lesions or abnormalities were assessed. Data were managed and analyzed using SPSS version-20. Mean and SD were reported for numeric data like age, BMI, and duration of TMF. Frequency and percentage were reported for categorical data like parity and gravida categories, family history of breast cancer, menopausal status, endometrial pattern, and the presence of any focal lesions or abnormalities. The distribution of pre and post TMF endometrial thickness was assessed using Shapiro-Wilk's test, which showed non-parametric distribution ($p<0.05$). The comparison between pre and post TMF endometrial thickness was done using Wilcoxon Sign Rank test. Level of significance was set at 5%.

RESULTS

The table 1 indicates that the mean age of the patients included in the study was 37.23 years, with a standard deviation of 7.16 years. The mean BMI of the patients was 26.05 kg/m^2, with a standard deviation of 3.26 kg/m^2. The duration of TMF was found to have a median of 24 months, with an interquartile range (IQR) ranging from 10 to 36 months. Most of the patients in were diagnosed with stage II breast cancer. Additionally, the majority of the female patients in this study had a history of multiple pregnancies (83.8%) and more than one childbirth (gravida >1, 13.8%). About 14.3% of the females had positive family history of breast cancer, and 75.3% had pre-menopausal status.

Table 1: Baseline characteristics of study variables (n=154)

Characteristics	
Age in years	37.23±7.16
BMI in kg/m^2	26.05±3.26
Duration of TMF (months)	24 (10-36)
Parity	
Nulli para	10 (6.5)
Single para	15 (9.7)
Multi para	129 (83.8)
Gravida	
0-1	25 (16.2)
2-3	68 (44.2)
>3	61 (39.6)

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Family history of breast cancer	
Yes	22 (14.3)
No	132 (85.7)
Menstrual status	
Pre-menopause	116 (75.3)
Post-menopause	38 (24.7)

Data presented as Mean ± SD or Median (IQR) or n (%)

The endometrial thickness pre-treatment and post-treatment was compared using Wilcoxon signed rank test, which revealed significant difference in both measurements. Thus, the TMF caused a significant increase in endometrial thickness with p-value=0.0001. Almost 80.5% of the females had endometrial thickness difference of less than and equal to 5mm and 19.5% of the females had endometrial thickness difference of greater than 5 mm, respectively as shown in Figure 1.

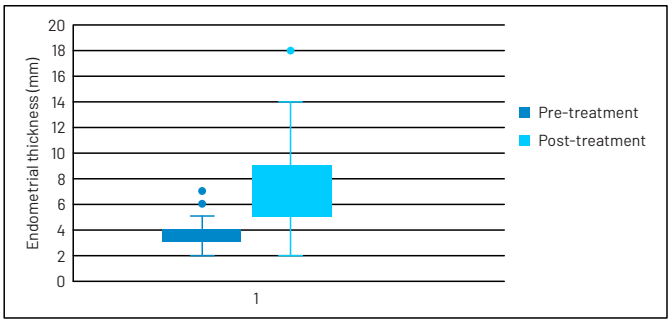

Figure 1: Comparison of pre and post treatment endometrial thickness

Among 154 females with breast cancer, polyps observed in 5 cases, those patients in which endometrial abnormality was seen undergone for biopsy to rule out malignancy. The findings seen on pathology after tamoxifen therapy were simple hyperplasia in 10, hyperplastic polyps in 5 and endometrial carcinoma in 4 cases.

DISCUSSION

The therapeutic approach of TMF has been extensively utilized in female patients diagnosed with breast cancer [11-13]. However, despite of having positive effects, it has been observed that TMF treatment can have detrimental effects on the uterus, leading to various benign and malignant changes [14]. This study was designed to investigate the risk of sonographic abnormalities in endometrium associated with tamoxifen use in breast cancer patients. Transvaginal ultrasonography was used as a method to evaluate endometrial status. The cut-off value of 5 mm on TVS was used to designate abnormally thickened endometrium since there have been several reports indicating that endometrial thickness greater than 5mm in breast cancer patient is associated with increase chance for endometrial abnormalities. Additionally, there is a potential risk of malignant transformation, leading to the development of endometrial carcinoma [15]. The present study showed that 5 cases had polyps, 10 cases had hyperplasia and 3 cases developed endometrial carcinoma. Similar study by Fishman *et al.*, found that 39% of females treated with TMF had endometrial polyps [15]. Another study by Love *et al.*, found that 3% of females with history of TMF use had endometrial cancer, 13% had endometrial hyperplasia, 44% had endometrial polyps, 2% had endocervical polyps, 17% had proliferative endometrium, and 21% had atrophic endometrium, respectively. Furthermore, 22% of the females had endometrial stripe thickness ≤4 mm [14]. While, study by Ryu *et al.*, revealed that females with breast cancer who had TMF therapy had greater incidence of polyps, endometrial hyperplasia, uterine cancers, and endometrial carcinoma as compared to adjuvant hormone therapy [4]. They also found that use of TMF was significantly associated with 4 times higher risk of developing endometrial cancer, even after adjusting for confounders i.e. BMI, age, dyslipidemia, hypertension, diabetes, GnRH agonist treatment and PCOs, respectively [4]. Another study revealed that polyps due to TMF use are found have a greater risk of malignant change compared to general population (10.7% vs 0.48%) [4]. Hetta *et al.*, found that 56% of the females had abnormal sonographic findings, wherein 4% had endometrial carcinoma, 14% had endometrial hyperplasia, and 7% had endometrial polyps, respectively [7]. We found that TMF caused a significant increase in endometrial thickness with p-value=0.0001. Furthermore, 19.5% of the females had endometrial thickness increased by 5mm after TMF use. While, in the study by McGonigle *et al.*, found that endometrial polyps were the frequent findings, along with endometrial cysts having endometrial thickness more than 5 mm [17]. In another study by Lee *et al.* 12% of the pre-menopausal and 10.6% of the post-menopausal women had endometrial thickness [6]. Another study by Jeon *et al.*, also concluded that endometrial thickness is significantly associated with endometrial pathology in breast cancer females treated with TMF [18]. Cohen *et al.*, also found endometrial thickness of more than 5mm in postmenopausal breast cancer females who were using TMF 20 mg/day for median duration of thirty-six months [19]. While, Lee *et al.*, found pre-menopausal breast females on TMF had significant association between endometrial thickness and endometrial cancer [20]. In another study by Parveen *et al.*, TMF showed positive correlation with uterine volume, endometrial thickness and abnormal findings as compared to females without TMF [21]. Hence, these finding suggests that the TMF treatment may have an effect on the proliferative properties of the endometrium. The study addresses an important clinical concern regarding the

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potential impact of TMF therapy on the endometrium in breast cancer patients. But the study has few limitations like the study is based on a single-center, quasi-experimental trial, which may limit the generalizability of the findings to a broader population. The study lacks a control group, making it difficult to establish a direct causal relationship between TMF use and the observed endometrial changes. The duration of TMF therapy varied among patients, which could introduce confounding factors and impact the interpretation of the results. The study relies on transvaginal ultrasound as the imaging modality for assessing endometrial changes, which may have limitations in detecting certain abnormalities compared to other imaging techniques or histo-pathological examination. However, the study utilizes transvaginal ultrasound, a widely accessible and cost-effective imaging modality, to assess endometrial changes, allowing for non-invasive monitoring during TMF therapy.

CONCLUSIONS

This study highlights the need for monitoring endometrial changes in breast cancer patients receiving TMF therapy. The findings suggest that TMF use may lead to an increased risk of endometrial pathologies, including polyps, hyperplasia, and carcinoma.

Authors Contribution

Conceptualization: AR[1], GH, M
Methodology: AR[1], GH, AR[2], DJ, NAB,
Formal Analysis: AR[2], DJ, NAB, KA
Writing-review and editing: AR[1], GH, M, KA

All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

The authors declare no conflict of interest.

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Original Article

Blood Donors Hemovigilance in Public Sector Tertiary Care Hospitals of Peshawar

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ABSTRACT

Hemovigilance of blood donors is an integral part of blood transfusion system, conferring to lessen the blood donation complications and enhancing the safety of blood donors. **Objective:** To determine the prevalence, severity, and associated factors of acute hemovigilance reactions in the blood donors of public sector tertiary care hospital bank banks in Peshawar. **Methods:** A multi-centered, cross-sectional approach was applied on blood donors` population selected via random proportionate sampling, visiting 6 Public sector tertiary care hospitals in Peshawar. Adverse reactions were reported on national guidelines reporting form during and after the blood donation. **Results:** Out of 420 blood donors selected via random proportionate sampling of total blood donors` population, prevalence of acute adverse hemovigilance reaction was 8.57% while no adverse reactions occurred in 91.43% of the blood donors. The most frequent hemovigilance reaction was vasovagal reactions (5.2%). All the reactions were of mild to moderate severity with no life threatening hemovigilance reactions. **Conclusions:** The overall prevalence rate was 8.57% of all healthy blood donors` which strengthens the fact that adverse reactions are avoidable complication of blood donations among the voluntary and replacement blood donors, and can be prevented with centralized hemovigilance data base for a sustainable base of voluntary blood donors.

INTRODUCTION

Hemovigilance has become an essential component of Blood Transfusion service (BTS) worldwide and has substantially contributed to the health systems of developed countries [1]. Blood Transfusion System in Pakistan is disintegrated and principally depends upon the replacement blood donors [2, 3]. Hemovigilance is proficient only in few blood bank facilities in Pakistan [4]. Approximately 3 million blood donors donate blood which is not enough to replenish the demand of drying blood banks in the country [5, 6]. The Blood Transfusion Services in the country were built upon the provincial legislations of Blood safety acts during 1997 till 2017 [7]. Pakistan became member of international hemovigilance network in 2013 February [5, 8]. The Khyber Pakhtunkhwa provincial assembly promulgated the Blood Transfusion Safety Authority Act XXV, on 20th October 2016, by establishing Khyber Pakhtunkhwa blood transfusion authority (KPBTA) with a principal focus on donor hemovigilance (section 18.1 & 18.2) [9-11]. The blood donor adverse reactions are categorized as localized or widespread. The localized reactions are majorly due to leakage of blood from veins after inaccurate venipuncture causing hematoma formation, nerve injury, pain, swelling and redness on the site of blood leakage [12-14]. The vasovagal reactions include dizziness, nausea, sweating, pallor, abdominal discomfort, low blood pressure, vomiting and decrease heartbeat. Whereas, systemic reactions may also lead to syncope or fall thus requiring prompt medical attention and

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management [15]. The main objective of this study was to determine the prevalence, severity, and associated factors of acute hemovigilance reactions in the blood donors of public sector tertiary care hospital bank banks in Peshawar. The acute adverse blood donation reactions have been studied extensively across the globe as depicted in Table 1.

Table1: Adverse blood donation reactions across the globe

S. no	Author	Year	Country	Prevalence/ Incidence of hemovigilance reactions
1.	Land *et al.*, [16].	2012-2017	United States of America	20.8 to 24.3/1000
2.	Notes *et al.*, [4].	2009	Italy	1.2%
3.	Zeiler *et al.*, [17]	2011	Germany	0.63%
4.	Newman *et al.*, [18]	2003	United States of America	7.8%
5.	Inaba *et al.*, [19]	2013	Japan	5.2%
6.	Wiersum-Osselton *et al.*, [14]	2014	Netherlands	3.9 -3.5%
7.	Charoonruangrit [20]	2013	Thailand	24.06%
8.	Kamel *et al.*, [21]	2010	United States of America	41/10000
9.	Agnihotri *et al.*, [22]	2012	Bangalore, India	2.5%
10.	Patidar *et al.*, [23]	2013	North India	18%
11.	Mahbub-ul-Alam *et al.*, [24]	2007	Bangladesh	4.98%
12.	Sultan *et al.*, [25]	2016	Karachi, Pakistan	1.3%
13.	Rohra *et al.*, [26]	2010	Karachi, Pakistan.	8.2%
14.	Amanat *et al.*, [27]	2015	Islamabad, Pakistan.	3%
15.	Shabber *et al.*, [28]	2016	Islamabad, Pakistan.	0.7%

METHODS

This was an analytical cross-sectional study conducted at the blood banks of Tertiary Care Hospitals in Peshawar. This study was conducted in 3 months interval from April 2021 till June 2021. The Quantitative research approach was adopted. It was a multicenter study, executed at the 6 Public Sector Tertiary care hospitals blood banks affiliated under the Regional Blood Center Peshawar. Khyber Medical University Advanced Study and Research Board (AS&RB) endorsed the study, Agreement of Helsinki Declaration (World Medical Association) [29] was maintained throughout the study [30, 31]. The target population in this study were the blood donors visiting the blood banks of tertiary care hospitals in Peshawar. The sampling technique was Random Proportionate Sampling. The total blood donor population recorded in these hospital blood banks were 66,624. The total sample frame was 420 which was collected proportionately from the 6 public sector tertiary care hospitals working under Blood Transfusion Authority Khyber Pakhtunkhwa. The sample calculation for a finite blood donor population through standard formula for sample size calculation was used. The selection criteria for blood donors were adopted according to the National guidelines in transfusion medicine [32], which includes: Age >18years, Weight >50kg, Hemoglobin levels>12.5g/dl, Blood pressure levels (systolic blood pressure not more than 140mmHg, diastolic blood pressure not more than 100mmHg). The general inclusion criteria included the willingness to participate in the study, after 1st 20min immediately post donation and 23hrs 40mins on telephonic interview after leaving the hospital blood bank through informed consent questionnaire duly signed by all the participants. For consideration of any potential blood donor deferral the National Guidelines for Quality Control in Transfusion Medicine deferral lists were followed [32]. Each donor was observed for development of adverse hemovigilance reactions during or after the blood donation of 1 pint or 500ml for at least 20 mins according to the national guidelines for quality control in transfusion medicine by trained staff of the hospital blood banks. The types of adverse hemovigilance reactions observed within 24 hrs. were noted through telephonic interviews for documentation on national transfusion medicine guideline adverse reaction reporting form. The blood donors were then classified into 3 age categories 10 years apart as: Category A (18-29 years), Category B (30-39 years), and Category C (40-49 years). The weight of blood donors was categorized into two groups: Group A (60-80kg), Group B (80-100kg and above). The hemoglobin levels were divided into two categories as: Category 1 (12-15gm/dl) and Category 2 (15-≥18gm/dl). The systolic blood pressure levels were categorized into 2 groups as: Group A (systolic blood pressure <100-119mmHg) and Group B (systolic blood pressure 120-139 mmHg). The adverse hemovigilance reactions were divided into 2 categories depending upon the onset of adverse symptoms in blood donors into: a) Acute immediate adverse hemovigilance reactions occurring within 20 mins after blood donation and b) Acute delayed adverse hemovigilance reactions occurring in 23hr 40min of blood donation. SPSS version 23.0 was used for the data analysis.

RESULTS

A total of 420 blood donors were enrolled in the study. A total of 97.61 % blood donors enrolled in the study were males while 2.38% of the blood donors were female. The mean age was 27.47±7.21 years. The mean weight(kg) of the blood donor was recorded as 76.78 ± 7.461 kg. A total of 208 (49.52%) blood donors were having different categories of occupation, while 212 (50.48%) were not working in any sort

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of occupation. The mean hemoglobin level was observed as 14.91 ± 0.7 gm/dl. The prevalence of acute adverse hemovigilance reaction was observed to be 8.57% while no adverse reactions were present in 91.43% of the blood donors. About 91.67% of the blood donors had no adverse hemovigilance reactions, 3.81% of the blood donors had experienced mild severity adverse reactions, 4.52% blood donors had experienced moderate adverse reactions. However, no severe and life threatening adverse hemovigilance reactions were observed. The most frequent acute immediate adverse hemovigilance reaction observed was systemic vasovagal reactions with or without loss of consciousness (5.2%), whereas nausea/vomiting (1%), weakness/hypotension (1.2%), and localized reactions such as hematoma and delayed bleeding (1.2%) as demonstrated in Table 2 as:

Table 2: Frequency of Acute immediate hemovigilance reactions among blood donors

Acute immediate adverse hemovigilance reactions (<20min)	Frequency (%)
No adverse reactions	384 (91.4)
Vasovagal reactions/syncope/faint	22(5.2)
Nausea /vomiting	4(1.0)
Hypotension/weakness	5(1.2)
Hematoma/delayed bleeding	5(1.2)
Total	420(100)

The most frequent delayed hemovigilance(adverse) reactions observed in blood donors was weakness, hypotension, and dizziness after blood donation. However no Systemic anaphylactoid reaction was observed during the blood donation process. the next frequent reactions noted in blood donors 23hr 40min post donation were localized reactions such as hematoma and delayed bleeding while delayed syncope/vasovagal reactions were the least frequent among blood donors as shown in Table 3 as:

Table 3: Frequency of Acute delayed hemovigilance reactions

Acute Delayed Hemovigilance Reactions Among Blood Donors (23hr 40min)	Frequency (%)
No adverse reaction	389 (92.6)
Delayed Vasovagal reactions/faint/nausea/vomiting	7(1.7)
Hematoma /delayed bleeding	9(2.1)
hypotension/dizziness/weakness	15(3.6)
Total	420(100)

Chi square test of association was applied to determine the significance of association as shown in Figure 1, a significant association of low weight categories (p=0.003 at 95% confidence interval and 0.05% margin of error) and lower hemoglobin levels (p=0.003 at 95% confidence interval and 0.05% margin of error) development of adverse hemovigilance reactions was found.

Table 4: Association of blood donors `demographic factors with development of acute hemovigilance reactions

Demographic Variables	Categories	Number (%)	Percentage of Adverse Reactions	p-value
Gender	Male	410(97.61%)	8.09%	0.191
	Female	10 (2.38%)	0.476%	
Occupation	Yes	208(49.52%)	4.076%	0.773
	No	212(50.47%)	4.52%	
Age	18-29 yrs.	271(64.52%)	5.47%	0.974
	30-39 yrs.	111(26.42%)	2.38%	
	40-49 yrs.	38(9.04%)	0.714%	
Weight	60-80 Kg	289	9.11%	0.003
	80-≥100Kg	95	0.26%	
Blood Pressure Level (Systolic)	<100119mmHg	150(35.71%)	4.04%	0.147
	120-139mmHg	270(64.28%)	4.52%	
Hemoglobin Level	12-15gm/dl	259	8.59%	0.003
	15-≥18gm/dl	125	0.78%	

DISCUSSION

The voluntary blood donations are the key force to maintain a sustainable blood donation supply to meet the blood demands of a country, which could be achieved through strict vigilance of adverse donation reactions at hospital blood bank. The overall prevalence of adverse reactions in, healthy allogenic blood donors visiting the Public Sector tertiary care hospital blood banks in Peshawar is 8.57%. This is the first baseline data from Khyber Pakhtunkhwa regarding blood donors from the Northwest frontier region inclusive of blood donors visiting from Afghanistan. The result of this study is in concurrence with a study steered at Karachi that reported vasovagal adverse donation reactions prevalence rate of 8.2% in healthy replacement blood donors [26]. In another study from Karachi by Sultan *et al.*, concluded an adverse reactions rate of 1.3% in allogenic healthy blood donors [25]. A relatively lower adverse donation reactions rate of 0.7% were reported in a study executed in a Tertiary care hospital in Islamabad [28]. The prevalence rate reported in this state are in accord with adverse donation reactions rate 24.06% in Thailand donors' surveillance program [20]. Whereas, a slightly higher prevalence rate 4.9% was observed in Bangladesh [24]. A relatively lower prevalence rate of 2.5% and 2.04% was recorded in a study in two studies in India [22]. A study from Italian blood transfusion centers enshrined a prevalence rate of 1.2% [14], while in Japan, only 2.8% blood donors experienced adverse hemovigilance reactions [19]. Meanwhile in Germany a prevalence rate of 0.63% was detected in elderly blood donors [17]. These variations in prevalence rates mainly attributes to the difference in demographic characteristics of blood donors. The most predominant acute hemovigilance adverse reaction observed in our study was vasovagal systemic reactions (5.2%) inclusive of syncope/faint occurring on site to blood

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donation. the vasovagal reactions are the most frequent acute hemovigilance reactions to blood donation in nearly 1-5% of all the blood donors [12]. A similar rate of vasovagal adverse events of 8.2% was enshrined by Rohra *et al.*, in a study executed at two hospital blood banks in Karachi, Pakistan [26]. The difference may be due to the sample size as in our study random proportionate sample was taken from all the public sector tertiary care hospitals. The vasovagal reactions account for 60.67% of overall acute adverse hemovigilance reactions (8.57%, n=420) which are somehow similar to an Indian studies vasovagal reactions (VVR) prevalence rates of 63.5% and 70.0%, [33]. The delayed adverse reactions after leaving the hospital blood bank and experienced >20min post donation and within 24 hours are recorded as 7.4% with hypotension /weakness as the most frequent delayed adverse hemovigilance reactions (3.6%) among all the blood donors. These prevalence rates are similar to a study by Kamel *et al.*, observed the delayed adverse reactions to be 12% that occurred offsite; elaborating the importance of follow up in blood donors through effective donors' surveillance system [21]. The findings in our study suggests that low hemoglobin levels and adverse donation events are significantly associated p=0.003 at 95% confidence interval and 0.05% margin of error ,which also support the results from other studies that blood donation related adverse reactions is a multifactorial process mainly demonstrated by factors such as young age, female gender, low weight, and first time blood donation status [34, 35] As demonstrated by Newman *et al.*, [18], the occurrence of adverse reactions are more likely in lower weight groups as stated in accordance with previous findings [36], and likewise demonstrated in a study in United States [37], which supports the findings of this study for determining the association of adverse events to weight categories the p=0.003 at 95% confidence interval and 0.05% margin of error. The female participants in current study were only 2.38% which is much less as compared to Italy where 30% of blood donors are female [38]. The overall female voluntary blood donors are <1 % of the total blood donor population in Pakistan according to the previous researches [26, 39]. However, our study revealed that there is no association between the adverse hemovigilance reactions and gender. The main reasons behind this lesser female proportion attributes to the paucity of information, cultural norms and increase misperception regarding adverse health outcomes in female blood donors. Hematoma and delayed bleeding along with hypotension/weakness constituted the 2nd most common (1.2%) of the overall adverse hemovigilance reactions in our study. These results settle with a study 2% from Bangladesh [24]. The findings are lesser as compared with the results of an Indian study by Agnihotri *et al.*, [22] which enshrined that 35% of all the adverse donors' events were localized hematoma. Another study from US which also elaborated a 15.1 % of the bruise /hematoma in blood donors The defective phlebotomy technique related localized adverse hemovigilance reactions occur 1 in every 6300 blood donors [40]. Moreover, the severity of all the adverse hemovigilance events in blood donors were of mild to moderate intensity predominantly. This also compliments the findings of other native studies which did not record any life threatening or severe intensity adverse reactions in their study [25, 28].

CONCLUSIONS

The overall prevalence rate of acute hemovigilance reactions revealed in our study was 8.57% of all the healthy blood donors` population taken from the public sector tertiary care hospital blood banks. It was learnt that no severe intensity acute hemovigilance reactions were observed during and after the blood donation thus strengthening the fact that blood donation is a harmless process. The adverse reactions are avoidable complication of blood donation which can be prevented through active surveillance during and after the blood donation process. Delayed adverse reactions are also prevalent among the blood donors but the nonexistence of baseline centralized data on delayed adverse hemovigilance reactions is a major unresolved hinderance for a sustainable base of voluntary blood donors for future blood demands.

Authors Contribution

Conceptualization: SN, AA
Methodology: SN, AA, BA, TN
Formal Analysis: SN, BA, TN
Writing-review and editing: SN, AA, TN

All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

The authors declare no conflict of interest.

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Original Article

Association between Socio-demographics of Nurses and their Knowledge about Hospital Waste Management in Tertiary Care Hospital Lahore

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ABSTRACT

The management of healthcare waste is very important due to the possible environmental dangers and threats to public health. Additionally, the direct exposure and handling of waste can results in disastrous events. Therefore, health care professionals should handle it carefully because majority of professionals does not give it importance to follow all the steps of waste management. **Objective:** To assess association between socio- demographics of nurses and knowledge about hospital waste management in Tertiary Care Hospital Lahore. **Methods:** A quantitative correlational study design was used for this study. The setting of study was Mayo Hospital Lahore. The study was completed in 3-month after approval of Ethical Research Committee. Sample size of 110 cases was calculated with 95% confidence interval. Data were collected by using Self developed demographic form and Knowledge Scale. Data were analyzed using SPSS version 24.0. **Results:** The result showed that among 110, the most of the participants are the age group of 31-40 years. Out of 110, majority of the participants (93.6%) are married. The study findings revealed that about 80(86.5%) participants had poor knowledge about hospital waste management and only 30(13.5%) nurses had good knowledge. Additionally, there was a statistically significant relationship between nurses' knowledge and their age, marital status, and qualification. **Conclusions:** It was concluded that majority of participants had poor knowledge regarding waste management. The knowledge of participants about waste management had statistically significant relationship with age, marital status, and qualification.

INTRODUCTION

Hospitals are organizations that offer a range of healthcare services to the general public [1]. They may provide patient care services that are curative, rehabilitative, preventative, and that also promote health education [2]. Hospitals and healthcare facilities have a responsibility to protect the public's health. This can be done directly by caring for patients or inadvertently by providing a clean, safe atmosphere for their staff and the general public [3]. All wastes produced by medical facilities, health research labs, and related facilities are referred to collectively as hospital waste (HW) [4]. Any solid or liquid waste from a hospital that might potentially infect people is considered hospital trash [5]. It is produced by healthcare institutions including hospitals that provide human treatment, diagnosis, or immunizations, blood banks, clinics, dental offices, and labs [6]. The waste of hospital is a unique kind of waste that, because of its infectious and/or poisonous qualities, is extremely dangerous [7]. Additionally, the risk associated with the handling of this sort of waste at health care facilities is increased by the direct exposure of waste management personnel and members of the public to it [8]. Despite the fact that there is variation in the handling of medical waste in different hospitals, but all healthcare facilities follow the same phases of waste management, which include separation, gathering, packing, preservation, transportation, treatment, and destruction

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[9]. To combat the hazards of hospital waste, the healthcare team member is seen to be the first line of defense [10]. The outcomes are devastating if this danger gets beyond the first line of defence. Therefore, the collaboration of healthcare team including nurses, physicians, and housekeepers is necessary to adequately address the risk of waste [11]. Where the system of healthcare waste segregation begins at the generational level. In order to properly manage medical waste, the members of the healthcare team must be well informed of all of its types, dangers, and management requirements [12]. There is a belief that the disposal of medical waste is only possible via the use of incinerators and various processing techniques [13]. However, this idea is incorrect; effective healthcare waste management relies on developing a medical waste treatment from the ground up. Inadequate treatment and improper treatment techniques to discard the waste can cause infection and serious diseases [14]. Regular staff practices need to be monitored in order to ensure that hospital trash is handled effectively over the long run. Waste management team should stress upon the proper handling of medical waste. Members of this committee are frequently the same people who oversee nosocomial infections. Therefore, highest standards should be practiced through appropriate training programmes [15]. However, major wards like the surgical and obstetrics departments are more prone to have an infection outbreak because there, patients may be exposed to infected surgical wounds. Nurses are immediately exposed to these risks since they are in charge of handling waste disposal [16]. The results of this study will pave the way for further research in this area and raise nurses' awareness of the significance of hospital waste management.

METHODS

A descriptive cross sectional research design was used to conduct this study. The current investigation was carried out in Mayo Hospital, Lahore. The study was conducted from August 2022 to October 2022 after getting the approval from Ethical Committee. A sample of 110 staff nurses was calculated using 95% confidence interval. Purposive sampling technique was used to collect the data. Nurses having age 20 to 40 year with at least one year of job experience were included in the study. Nurses with mental illness and aged above 40 year were excluded from study. The level of knowledge of respondents was assessed by 16 multiple choice questions [1]. The total score ranged from 0-16. Each correct answer was marked as 1 and wrong answer. Based on blooms cut off points, the knowledge of respondents was categorized as poor with 0-16 scores with 40% correct answers, average knowledge with 7-12 scores with 41%-75% correct answers, and good knowledge with 13-16 scores with 76%-100% correct answers [17]. Data were collected from nurses from all major departments of Mayo Hospital Lahore. All participants were given a brief explanation of the study's goal by the researcher. After obtaining written, informed permission, a self-administered questionnaire related to demographic characteristics and related to waste management was distributed among participants. Seventy percent of the participants returned filled performa and 30% did not returned the questionnaire. They returned it after one week. SPSS version 24.0 was used to analyze the data. The demographic information was calculated using descriptive statistics (frequency and percentages). The connection between participant knowledge and demographic factors was examined using the Chi Square test.

RESULTS

A total of 110 participants participated in study. Data about demographic characteristics and knowledge about waste management is given in tables below. The socio-demographic features of the nurses under study are shown in Table 1. The table demonstrates that 110 nurses took part in this study. With a mean age of 34.37.8 years, 63.6% of them were above the age of 30. Nursing staff who were married (93.6%) made up the majority. And 73.6% had a graduate degree in general nursing. All of the nurses were enrolled in waste management training programmes, and more than half of them (71.8%) had experience spanning more than five years.

Table 1: Demographic characteristic of participants

Variables	No. (%)
Age	
20-30 year	40 (36.4)
31-40 year	70 (63.6)
Range	23.0-59.0
Mean ± SD	34.3±7.8
Median	32.0
Gender	
Male	27 (26.4)
Female	83 (73.6)
Marital Status	
Single	7 (6.4)
Married	103 (93.6)
Religion	
Muslim	82 (76)
Christian	28 (24)
Nursing qualification	
General Nursing Graduate	81 (73.6)
Post RN BSN	29 (26.4)
Experience years (total)	
<5	31 (28.2)
5+	79 (71.8)
Range	2.0-39.0

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Mean ± SD	15.2±8.1
Median	13.5

The study's nurses' stated overall knowledge of hospital waste management is summarized in Table 2. As the table demonstrates, all nurses were familiar with general safety measures and trash transportation, but only 30 (13.5%) of them were knowledgeable about hospital waste management. In contrast, 80 (86.5%) nurses had inadequate hospital waste management knowledge.

Table 2: Knowledge of participants regarding waste management

Level of Knowledge	Frequency (%)	Valid Percent
Poor Knowledge	80 (86.5)	86.5
Good Knowledge	30 (13.5)	13.5

Table 3 shows the relationship between the personal and professional traits of nurses and their understanding of hospital waste management. The data shows that nurses with sufficient expertise were over 30 years' old, female, post-RN BSN holders, and had more than 10 years of experience in the nursing industry. Additionally, the table shows that there is a significant relationship between a knowledge of nurses and demographic variable e.g. age, marital status, and qualification as p value is less than 0.05.

Table 3: Relationship between socio-demographic factors and knowledge of nurses about hospital waste management

Demographic Characteristics	Knowledge score				X^2 test	p- value
	Poor		Good			
	No.	%	No.	%		
Age						
<30	12	30.0	28	70.0	3.93	0.047*
30+	10	14.3	60	85.7		
Gender						
Male	2	2.6	5	71.4	Fisher	0.63
Female	20	19.4	83	80.6		
Marital Status						
Single	22	35	30	45	9.006	0.024
Married	10	15	2	3		
Religion						
Muslim	12	25.0	36	75.0	1.33	0.25
Christian	10	16.1	52	83.9		
Nursing qualification						
General Nursing Graduate	21	25.9	60	74.1	6.74	0.01*
Post RN	1	3.4	28	96.6		
Experience years (current)						
<5	12	25.0	36	75.0	1.33	0.25
5+	10	16.1	52	83.9		

DISCUSSION

Healthcare institutions have a duty to safeguard the environment and the general public's health. The purpose of this study is to ascertain the participants' level of awareness regarding hospital waste management. The results of the current study shows that the majority of nurses were married, were older than 30 years old, and varied in age from 23 to 59 with a mean age of 34.17.8. An investigation done in Pakistan have similar findings and reported that age of majority of participants between 16 to 30 years [18]. The majority of them had general nursing graduate degrees and more than ten years of nursing experience. In contrast a study conducted in Iran revealed that majority of the participants had clinical experience greater than 5 year [4]. While addressing the knowledge of nurses about hospital waste management, the current study reported that a large number of participants (86.5%) had poor knowledge about hospital waste management. This is because, in Pakistan infection control team in hospitals is failed to supervise the practices of medical and non-medical professionals to improve their practices of handling the waste. Hospital management should arrange waste management orientation programme for employees, handouts of waste management, and training sessions on regular basis. In contrast, a research conducted in India, reported that nurses working in three hospitals had average knowledge about waste management [19]. Similar to this, Sobh revealed that 85% of nurses in India have strong awareness of biomedical waste management [1]. In addition, a research conducted in Nigeria reported that 95.8% of nurses had good understanding of biomedical waste management and its techniques [20]. In the same direction, a South African research assessed doctors' and nurses' practises and understanding of biological waste management revealed that 90% of respondents had limited expertise [21]. While these results were in contrast to those of Elsayed *et al.*, who discovered that about 98.7% nurses had good information regarding waste management at Mansoura University Hospital [22]. Additionally, a research in Christian Mission Hospitals in Madurai revealed that only a minority (25%) of participants have strong expertise, which is comparable with the findings of the current study [23]. Similar findings were made by Adu (2020), who discovered that study participants had an unacceptable mean knowledge score of 45.5±10.52 [24]. The current study revealed that there was a significant correlation between nurses' knowledge and their age, marital status, and qualification. This indicates that nurses with increased age and qualification had better understanding about biomedical waste. The fact is that senior nurses in the hospital system had better practice to handle the waste. This concurs with a research from Iran that shown that nurses with more years of experience become more informed, skilled, and confident in their ability to seek a level of excellence [25]. These results are consistent with those of Dey and Das who found that Indian nursing

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professionals' understanding of Bio Medical Waste is significantly associated with age and experience [26]. In contrast, Al-Khatib demonstrated that staff nurses' awareness of hospital waste was unaffected by their years of experience [27]. Additionally, a research done in India found a link between personal traits and nurses' expertise that was detrimental [28].

CONCLUSIONS

According to the study's findings, just 20% of nurses had high understanding of waste management in hospitals, while 80% of nurses had inadequate knowledge. Additionally, there was a significant association between knowledge of nurses and age, marital status and qualification of nurses.

Authors Contribution

Conceptualization: TW, MI, AS
Methodology: SK
Formal analysis: NR
Writing-review and editing: TW, MI, AS, SK, NR

All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

The authors declare no conflict of interest.

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Original Article

Association of Diet Consumption with Gallbladder Changes in Females After Birth of Child

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ABSTRACT

The postpartum period is characterized by remarkable physiological adaptations to accommodate the demands of childbirth and lactation. These physiological changes, coupled with the unique nutritional needs of both the mother and newborn, can lead to gallbladder stasis and increased cholesterol absorption in the gallbladder. **Objective:** To assess the correlation between diet consumption and gallbladder changes in females after childbirth. **Methods:** This observational study was conducted at the department of Gastroenterology, Jinnah Medical and Dental College, Sohail University, Karachi, Pakistan from December 2022 to June 2023. Females of reproductive age who had normal child delivery were evaluated after 6 weeks of delivery. The medical examination, anthropometric measures, nutritional assessment, and laboratory testing were performed in all eligible females. An ultrasonographic was done after a typical fatty food in order to assess gallbladder changes. SPSS version 21.0 was used to do statistically analysis. **Results:** The mean age was 28.89 ± 4.73 and mean BMI was 22.78 ± 4.09 kg/m^2. Of 100 females, 17% had gallbladder stasis, 26% had gallstones, and 17% had sludge. The females with low protein consumption had significantly higher proportion of gallbladder stasis as compared to females with high protein consumption in diet (76.5% vs 23.5%, p=0.001). Furthermore, females with high carbohydrate (61.5% vs 38.5%, p=0.011) and fructose (53.8% vs 46.2%, p=0.037) consumption had significantly higher proportion of gallstones as compared to females with low consumption. **Conclusions:** High protein consumption was linked to gallbladder stasis, while high carbohydrate and fructose intake were associated with an increased proportion of gallstones.

INTRODUCTION

Gallbladder disorders, particularly cholelithiasis, have emerged as significant health concerns affecting millions of individuals worldwide, especially females [1]. The prevalence of gallstone disease varies among different countries. Approximately 10% of individuals residing in Western countries and 5% of those in underdeveloped nations such as Pakistan experience cholelithiasis [2]. Evidence showed that gallstone disease is linked to a range of potentially life-threatening consequences, including gallbladder cancer [3]. Cholelithiasis is the 2nd most frequent emergency during or shortly after delivery and the leading cause of maternal re-admission in the first two months after delivery [4, 5]. Around 8% of the pregnant females develop new gallstones by the third trimester, and only about 1% experience symptoms. Among those who do experience symptoms, less than 10% encounter complications [6]. The postpartum period is characterized by remarkable physiological adaptations to accommodate the demands of childbirth and lactation [7]. These physiological changes, coupled with the unique nutritional needs of both the mother and newborn, can lead to gallbladder stasis and increased cholesterol absorption in the gallbladder [8, 9]. In a large study on pregnant females, it has been observed that high fructose and carbohydrate consumption increases the risk of gallstone [10]. In Pakistan, a significant portion of females being treated for

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gallstones are slender, undernourished, multiparous young women from lower socioeconomic backgrounds [11]. Understanding the potential risk factors contributing to gallstones in this particular demographic can aid in the development of preventive measures and offer valuable insights into the etiology of gallstone disease. Hence, the aim of current study was to assess the association between gallbladder changes and nutritional deficiencies in females after childbirth.

METHODS

This observational study was conducted at the department of gastroenterology, Jinnah Medical and Dental College, Sohail University, Karachi, Pakistan from Dec 2022 to Jun 2023. Sample size of 98≈100 females was estimated using Open Epi sample size calculator by taking statistics of incidence of gallbladder as 10.2% in pregnant females [10], a bound-on error as 6% and 95% confidence level. The study included postpartum females aged above 18 years who had given birth to a single live infant at full term. Females with frequent pancreas inflammation, biliary distress syndrome, prior cholecystectomies, and complications such as congenital defects, restricted intrauterine growth, stillbirths, or multiple gestations were excluded. Non-random purposive sampling technique was employed for participant selection. Ethical approval for the study was obtained from the ERC of Sohail University, and informed consent was obtained from all eligible females. Data on demographics, medical history, anthropometric measures, and dietary intake were collected. Dietary intake was assessed using a meal frequency questionnaire, and a comprehensive nutritional evaluation was performed, with special emphasis on carbohydrate, fructose and protein consumption per day. Consumption of carbohydrate > 210 g/day, fructose > 25 g/day and protein >100 g/day were labelled as high consumption. Gallbladder (GB) function was evaluated using real-time ultrasound imaging conducted by a GI radiologist with over 5 years of experience. Participants were required to fast overnight for the study, and GB volume was measured using the ellipsoid technique. After consuming a common fatty meal, GB emptying was assessed by capturing ultrasound images of the GB at specific intervals, enabling the calculation of variables such as basal volume, ejection fraction at various time points, and the duration for the greatest constriction. Data were analyzed using SPSS version 21.0. Descriptive analysis of numeric and categorical data were performed. Frequency and percentage were computed for parity, gestational diabetes mellitus, pregnancy-related hypertension, dietary consumption, family history of gallstones, biliary symptoms, gallbladder stasis, gallstones, and sludge. Mean and Standard Deviation were reported for age, BMI, gallbladder volume left over after 60 mins, fasting volume in the gallbladder, gallbladder ejection fraction. Comparison between gallbladder changes and dietary intake was done using Chi-square/Fisher Exact test. A p-value less than and equal to 0.05 was considered as statistically significant.

RESULTS

The mean age was 28.89 ± 4.73 and mean BMI was 22.78 ± 4.09 kg/m^2. Most of the females were multiparous (88%), 3% had gestational diabetes mellitus, 12% had pregnancy-related hypertension and 2% had family history of gallstones (Table 1). Biliary colic was the most frequent biliary symptom during pregnancy (10%), followed by itching (6%), cholestasis (5%) and jaundice (1%), respectively. The mean gallbladder volume left over after 60 mins was 12.08 ± 1.82, mean fasting volume in the gallbladder was 20.58 ± 2.68, and mean gallbladder ejection fraction was 50.67 ± 10.26. Of 100 females, 17% had gallbladder stasis, 26% had gallstones, and 17% had sludge.

Table 1: Baseline characteristics of study variables (n=100)

Characteristics	Statistics
Age (years)	28.89±4.73
BMI (kg/m2)	22.78±4.09
Parity	
Nullipara	4 (4)
Single para	8 (8)
Multipara	88 (88)
Gestational diabetes mellitus	
Yes	3 (3)
No	97 (97)
Hypertension	
Yes	12 (12)
No	88 (88)
Family history of gallstones	
Yes	2 (2)
No	98 (98)
Data presented as Mean ± SD or n (%)	

The females with low protein consumption had significantly higher proportion of gallbladder stasis as compared to females with high protein consumption in diet (76.5% vs 23.5%, p=0.001). Furthermore, females with high carbohydrate (61.5% vs 38.5%, p=0.011) and fructose (53.8% vs 46.2%, p=0.037) consumption had significantly higher proportion of gallstones as compared to females with low consumption (Table 2).

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Table 2: Comparison of diet intake and gallbladder changes during pregnancy

Diet	Gallstones	Sludge	Gallbladder stasis
Consumption of protein			
High (n=40)	12 (46.2%)	8 (47.1%)	13 (76.5%)
Low (n=60)	14 (53.8%)	9 (52.9%)	4 (23.5%)
p-value	0.457	0.514	0.001*
Consumption of carbohydrates			
Low (n=21)	10 (38.5%)	1 (5.9%)	5 (29.4%)
High (n=79)	16 (61.5%)	16 (94.1%)	12 (70.6%)
p-value	0.011*	0.093	0.343
Consumption of fructose			
Low (n=30)	12 (46.2%)	7 (41.2%)	8 (47.1%)
High (n=70)	14 (53.8%)	10 (58.8%)	9 (52.9%)
p-value	0.037*	0.271	0.092

DISCUSSION

The present study aimed to assess the association between gallbladder changes and diet in females after childbirth. The results indicate that gallbladder disorders are not uncommon in the postpartum period, with a considerable proportion of women experiencing gallbladder stasis, gallstones, and sludge. These findings are in line with previous studies that have reported an increased risk of gallstone formation during and after pregnancy, particularly in females with certain dietary habits [10, 12, 13]. In our study, the incidence of gallstones aligns with global estimates, with almost 26% of pregnant females have cholelithiasis [2, 14, 15]. Six weeks after giving birth, we found that these women had a higher incidence of gallbladder stasis, which refers to a reduced flow of bile from the gallbladder. This condition was associated with several other factors, including a lower ejection percentage (indicating impaired gallbladder function), larger baseline gallbladder volumes, and slower responses to fatty meals. It is essential to address this issue to improve maternal health and reduce maternal re-admissions related to gallbladder complications. Although earlier research has indicated that in women who are pregnant average basal levels are around 70% greater than those of non-pregnant supervises, the volumes revert to baseline as soon as two weeks after delivery [16, 17]. Yet, at just six weeks after giving birth, our patients showed higher volumes and stasis, which could have been related to their diet's lack of protein, low BMI, or concurrent lack of iron. Additionally, the study revealed a significant link between inadequate carbohydrate and calorie consumption and an increased prevalence of gallstones in postpartum females. Those with high carbohydrate and calorie intake had a 61.5% and 53.8% occurrence of gallstones, respectively, compared to 38.5% and 46.2% in those with low consumption. The majority of the females, we discovered, consumed more carbohydrate and less protein than what was advised for women in the postpartum period [18, 19]. This observation corresponds with previous studies that have reported a positive correlation between gallstone formation and low-fat diets [20-22]. A study by Park *et al.*, also suggested an association between fatty foods and increased risk of gallstone development [23]. Hence, high protein intake has been associated with increased cholesterol saturation in the bile, which can lead to the formation of gallbladder sludge and stasis. On the other hand, diets rich in refined carbohydrates and high fructose intake can lead to insulin resistance and altered lipid metabolism, contributing to gallstone formation [21, 23, 24].

CONCLUSIONS

High protein consumption was linked to gallbladder stasis, while high carbohydrate and fructose intake were associated with an increased proportion of gallstones. These findings underscore the importance of promoting a balanced diet during and after pregnancy to mitigate the risk of gallstone-related complications in vulnerable populations.

Authors Contribution

Conceptualization: AAR
Methodology: SSR, JU
Formal analysis: SSR, JU
Writing-review and editing: AAR, SSR, JU

All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

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Original Article

Association Between Screen Time and Tear Film Stability

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ABSTRACT

Tear film is a layer that nourishes, lubricates and protects the anterior surface of eye. The usage of electronic gadgets can affect the tear film stability causing ocular dryness. Recently, due to the increased frequency of online educational and leisure activities, there has been reported increase in the prevalence of dry eye among users of electronic gadgets. **Objective:** To evaluate association between screen time and stability of tear film. **Methods:** A descriptive cross-sectional study was conducted from January to august 2021 at The University of Lahore. 120 participants aged above 18 years were recruited using nonprobability sampling technique. After taking consent from the participant's questionnaire was completed, followed by slit lamp examination for evaluation tear film breakup time (TBUT). **Results:** 120 healthy people of either gender who were at least 18 years old participated in this study, selected through random sampling, informed consent was acquired from all participants. The TBUT test was performed on all subjects, 74 had severe dry eyes, 21 had moderate dry eyes, and just 24 had normal eyes. Each subject's screen time was tracked after the subjects were divided into four groups. The Chi square was used to assess the relationship between screen time and tear film break up time. Results had a p value less than 0.01 and were statistically significant. **Conclusions:** This study concluded that as the screen time increases it effects the stability of tear film.

INTRODUCTION

An important component of ocular surface is tear film (TF) as it maintains ocular surface health. This (TF) is made of three layers and there is no barrier between these layers. It is not secreted as complete solution; different glands secrete different layers of tear film [1]. It is composed of Mucin, Enzymes, glycoproteins, immunoglobulins, lipids, electrolytes and water [2]. TF is a crucial component of ocular protection., there are number of factors such as extreme temperature, antimicrobial components in tear film helps to protect the ocular surface from infection and can be severely affected by irritants and allergens [3]. It has three layers, including an outer lipid layer, an aqueous middle layer and innermost mucus layer over the 1st layer of cornea [4]. The lipid layer which is the most outer layer provide a smooth surface and retard the rate of tear evaporation from the cornea [5]. The aqueous layer, which is made of water and helps the tear film spread, gives the cornea oxygen and nutrients [6]. The accessory lacrimal glands, such as the wolfring and Krause glands, are responsible for the basal secretion of the second layer of tear film [7] whereas the primary lacrimal gland is responsible for reflex tear film secretion. This layer is mildly alkaline and has an osmolarity of 300 mOsm/l [8]. The tear film's innermost layer acts as an anchor and promotes tear film adhesion to the eye [9]. It is important for protection of anterior corneal surface, act as a polish for cornea. One of the most significant characteristics of tear film is its stability, which is required for ocular surface protection. All

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of the tear film's components and layers, such as the lipid layer, aqueous layer, and mucin layer, must be present to keep the tear film stable [10]. Tear film not only protects from dryness, infection it also maintains the transparency of cornea and is essential for the optimal functioning of the eyes. It nourishes, lubricates and protects anterior surface of eyes. Tears are continuously absorbed and evaporated from the ocular surface [11]. When digital devices are excessively used then blink rate decreases significantly because of which Meibomian glands are not sufficiently stimulated to release the tear film's lipid layer [12]. The use of computers, laptops, tablets, and smartphones has steadily increased over the past few years with the passage of time and the development of technology [13]. The intermediate holding distance required by these digital devices puts pressure on the visual system, which is designed for comfortable near and distant vision [14]. The use of these electronic devices has significantly increased during the previous few years [15]. According to optometric association two hours of continuous screen time per day is enough for causing eye related problems like decrease blink rate and dryness [16]. Digital eye strain is a manifestation of evaporative dry eye it is increased in COVID pandemic [17] as the whole learning system has been shifted to the online classes and are using their tablets, mobiles and laptop more often for educational as well as sports/leisure time [18].

METHODS

From January 2021 to August 2021, 120 (n=z2pq/e2) subjects selected through convenient sampling were included in this descriptive cross-sectional study conducted at The University of Lahore. All the subjects with age limit 18-30 were included. patients with mental retardation, systemic, congenital, or ocular disorders were excluded, as well patients who had undergone any eye surgery or who had worn contact lenses. Each subject's proper informed consent was obtained. Depending on their age, patients were placed into three groups. Group 1 includes respondents between the ages of 18 and 21; Group 2 includes subjects between the ages of 22 and 25; and Group 3 includes subjects between the ages of 26 and 30. Data were collected from the subjects with the help of self-designed Performa The Performa was created to gather data regarding screen time. After taking proper history, Performa was administered to evaluate subjects screen time then tear film stability was examined by tear film break up time in which fluorescein dye was instilled in eyes then subject is instructed to not blink adjust patient on slit lamp and start examining on cobalt blue illumination The length of time between the final blink and the appearance of the first dry area in the tear film is known as the tear break up time. Three categories are used to classify tear film breakup times. Less than five seconds are regarded as low, between five and ten seconds as marginal, and more than ten seconds as normal. SPSS version-21.0 was used to analyze the data.

RESULTS

This study consisted of both eyes of 120 normal subjects of either gender aged above 18years from all subjects informed consent was obtained. The overall number of subjects in Group 1 (18 to 21 years), Group 2 (22 to 25 years), and Group 3 (26 to 30 years) was 37 (30.8%), 50 (41.7%), and 33 (27.5%), respectively. A total of 57 females and 63 guys made up the sample. Males were more common than females (52.5% vs. 47.5%), by a wide margin. TBUT test was performed on all 120 subjects out of which 79(65.8%) had severe dry eye while 26(21.7%) had moderate dry eye and only 15(12.5%) subjects were normal. Screen use of total 120 subjects were divided in to four categories, screen time was measured in 120 subjects out of which 79(63.3%) had screen time more than 8 , 24(21.7%) subjects had screen time more than 6 hours, 12 subjects had screen time of 3-5(10.0%) hours while on only 8(6.7%) subjects had screen time less than 1-2 hours. Chi square was used to assess the relationship between screen time and tear film break up time. Chi square shows significant p value < 0.01 relationship between screen time and tear film stability. It means as the screen time increases it effects the stability of tear film. Total 120 subjects were included in this study of either gender male or female age ranging from 18 above years of age. All individuals were divided in to three age groups. Total 37 subjects were lies in 18-251 years of age. 50 individuals are in group 22-25 and only 33 subjects were presented with ages 26-30 year of age. As shown in table 1.

Table1: Frequency of age of different individuals

Age	Frequency (%)
18-21 years	37(30.8)
22-25years	50(41.7)
26-30 years	33(27.5)
Total	120(100)

Figure 1 shows total 120 subject are involved in this study. out of 120 subjects total 63 males (52.5%) frequency and females are 57 (47.50%) were undergone TBUT measurements.

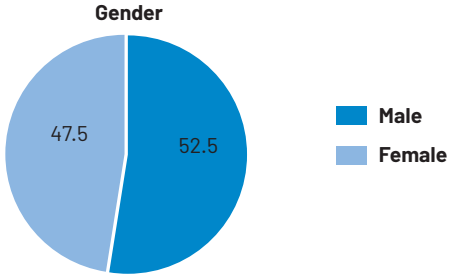

Figure 1: Frequency of gender included in study

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Table 2 shows chi square analysis of total 120 subjects were included on which TBUT was performed on screen users, divided into 3 categories. (74) subjects having screen time of more than 8 hours have sever tear film instability (< 5 seconds), 21 subjects having screen time more than 6 hours have moderate tear film instability (5-10 seconds), 24 subjects having screen time more than 6 hours are normal (>10 seconds). Study shows significant results (p<0.01).

Table 2: Chi square test was applied to assess the relationship between screen time and tear film Stability

TBUT	1-2 hours (less)	3-5 hours (moderate)	>6 hours (high)	>8 hours (high risk)	Total	p-value
< 5 seconds (Low)	0	1	3	74	79	0.01
5-10 seconds (Marginal)	2	3	21	0	26	
>10seconds (normal)	6	8	0	1	15	
Total	8	12	24	75	120	

DISCUSSION

In this clinical research we assessed the relationship between screen time and tear film stability, screen time was assessed by self-designed Performa while tear film stability was assessed by tear film break up time. Screen time was divided into 4 categories while tear film stability was divided into three categories. Our study shows significant relationship (p=<0.01). In 2021, Verma *et al.*, did a cross-sectional study at a teaching institute to determine the prevalence of computer vision syndrome and dry eye in computer operators. One hundred participants were included in the study based on the inclusion criteria [19]. A questionnaire was created to enquire about CVS symptoms. The Ocular Surface Disease Index (OSDI), refraction, Schirmer's test 1, and tear film break-up time (TBUT) were all carried out. The data were gathered and analyzed using SPSS software. 74% of people were found to have CVS. 39 women and 61 men made up the study's sample size. Depending on the working hours, the majority of the participants (37.84%) worked 4–8 hours every day. 37.84% of participants who worked between 4 and 8 hours did so. According to the OSDI score, 41 individuals had moderate dry eye and 23 individuals had mild dry eye. 58% of the left eye and 59% of the right eye both had dry eyes. The study's conclusion is that the prevalence of dry eye has increased as a result of the increased use of computers in daily lives. Similarly, in our study120 subjects those who were screen users, divided into 3 categories. (74) subjects having screen time of more than 8 hours have sever tear film instability (<5 seconds), 21 subjects having screen time more than 6 hours have moderate tear film instability (5-10 seconds), our study co relate with results of our study that screen time has significant effect on tear film stability [19]. Peak Kyung's study, which he conducted among college students to evaluate the association between addictive smart phone use, dry eye syndrome, upper extremity discomfort, and depression, produced results that were in agreement with those of our study. A self-report questionnaire was utilized to gather data from 286 college students for this study. 15.0 % of people reported having a smartphone addiction. Our study likewise came to the same conclusion that increasing screen time has a serious negative impact on eyes, inducing dryness, comparable to his study's conclusion that addicted smart phone use has large disparities in dry eye [20]. Our findings were consistent with a study conducted by Loebis *et al.*, on the relationship between exposure time to mobile devices and the prevalence of evaporative dry eyes as one of the symptoms of computer vision syndrome among Senior High School Students. The data show that 94 students participated in this study. There were 82 students overall who had evaporative dry eyes (87.2%). Thirteen kids (11.7%), 18 students (19.1%), and 53 students (56.4%) had dry eyes as a result of low exposure, moderate exposure, or high exposure, respectively. A chi square analysis revealed that all HEV exposures have a comparable likelihood of resulting in dry eyes in high school students (p 0.05). This study found that even minimal exposure to mobile devices may increase the risk of developing evaporative dry eyes, one of the symptoms of CVS in young persons with normal tear production [21].

CONCLUSIONS

According to my study there is greatest statistical significance between screen time and dry eyes. Stability of tear film greatly decrease with the increased screen time(p<0.01). Results of study concluded that screen time has significantly increased during COVID time which has greatly affected the stability of tear film and daily number of students are reporting to clinical set ups with the problem of dry eye.

Authors Contribution

Conceptualization: MZ
Methodology: MR
Formal Analysis: HI
Writing-review and editing: MZ, MR, HI

All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

The authors declare no conflict of interest.

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Original Article

Knowledge of Pregnant Women Regarding the Mode of Delivery among the Primary Gravida

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ABSTRACT

Caesarean sections (CS) are becoming more commonplace. Pregnant women's awareness of childbirth options, the causes contributing to their lack of information, and their desire for CS delivery were little understood. **Objective:** To assess the knowledge of pregnant women regarding the mode of delivery among the primary gravida. **Methods:** A descriptive cross-sectional research study design was conducted at Jinnah Hospital Lahore during January to June 2023. About 171 pregnant patients were enrolled to assess the knowledge of pregnant women of the first gravida. Data analysis was done through (SPSS) version 21.0. The Bartlett and KMO values have been checked to ensure validity and reliability in our context. **Results:** Out of 171 pregnant females, 90.6% were aged 21-30 years. Approximately 67.3% believed that vaginal birth is a natural and appropriate way of delivery, and 87.7% believed that the infant might be obtained early within minutes by vaginal delivery. About 88.3% females thought that vaginal delivery is better than cesarean section, however 85.5% also thought that it is also risky for baby. **Conclusions:** Generally, the knowledge of pregnant women about the mode of delivery and benefits of vaginal delivery is good in this study. But due to their thought about risk to the fetus, mostly select cesarean section over vaginal delivery. Therefore, the patient should be educated about the knowledge of pregnant women's mode of delivery to control the (CS) rate.

INTRODUCTION

Birth via caesarean section is performed by making an incision in the mother's abdomen (laparotomy) and uterus (hysterectomy) to deliver the fetus. The procedure has come a long way since the first caesarean section in 1020. In Pakistan, nearly a million women have their infants through caesarean section each year, making it the most popular treatment in the country. From a rate of 5 per 100,000 births in 1970, it reached 31.9 in 2016 [1]. Despite continuous efforts, doctors do not anticipate a significant drop in the rate of caesarean sections for at least another decade. Some women may not have any other choice than to have a caesarean delivery, despite the potential for both immediate and long-term complications [2]. Vaginal delivery is the safest choice for both the fetus and the mother when the pregnancy reaches full term, between 37 and 42 weeks [3]. Vaginal birth is favored over surgical birth because of the increased risks of complications and death that come with caesarean sections. Eighty percent of all singleton vaginal deliveries occur at full term with the help of robotic labor [4]. There are eleven preterm births and ten full-term births. In particular, the number of patients progressing to robotic labor has reduced over time due to the advent of operational and surgical delivery methods, while the number of cases requiring induction of labor has grown [5]. Reduced mother and newborn morbidity and death might result from fewer needless caesarean

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sections if more women were educated about the risks and benefits of this delivery method. For improved gap identification, community and case awareness, and patient agency, investment in this area of patient care is essential [6]. The maternal mortality rate (MMR) in Pakistan was reduced by three-quarters between 1990 and 2015, while the under-five mortality rate (U5MR) was reduced by two-thirds. Both of these goals were part of the Millennium Development Goals (MDGs). The current prevalence of CS is far greater than the 10–15 percent target set by the WHO [7]. Pregnant women's knowledge of the mode of delivery and the factors that may influence their preference for CS delivery will be used by policymakers and healthcare providers to design effective programmes and interventions with the goal of reducing CS deliveries for better maternal and child health outcomes [8]. The purpose of this research was to determine how well women, particularly first-time mothers, understand the advantages of vaginal birth and the drawbacks of caesarean section. In order to encourage more women, particularly first-time mothers, to give vaginal birth a try and minimize the frequency of needless caesarean sections.

METHODS

From January 2023 to June 2023, a descriptive cross-sectional research was conducted at the Jinnah Hospital's Department of Obstetrics and Gynecology in Lahore. There were 171 participants in this trial. Using a 95% confidence interval, a 7% margin of error, and the proportion of caesarean sections (31.9%), a sample size was determined [1]. Females were enrolled who fulfilled selection criteria below by using simple random sampling. The study targeted population were the primigravida females of age 18 – 40 years, presenting for antenatal booking at gestational age >8 weeks. Those women with any risk pregnancy including chronic or gestational hypertension, diabetes, anemia, morbidly obese, low lying placenta, twin or multiple gestation were excluded from this study. Then females were asked about vaginal delivery and its pros and cons by researcher. A pre-designed proforma was used to gather the information and responses of females. Data analysis was done through statistical package of social sciences (SPSS) version 21.0. Frequency and percentage were used to present responses of females.

RESULTS

Table 1 shows that from total no of participants who responded in this study, those with the age group 18-20 year were 8(4.7%) those with the age group 21-30 year were 155(90.6%) and those age group 31-40 year were 8(4.7%). Those who had primary education were 86(50.3%) and those who had secondary education were 81(47.4%).

Table 1: Basic demographics of patients (n = 171)

Demographics	Frequency (%)
Age	
18-20	8 (4.7)
21-30	155 (90.6)
31-40	8 (4.7)
Education	
Primary	86 (50.3)
Secondary	81 (47.4)
All ability of schools	4 (2.3)

Table 2 shows that from total no of participants who responded in this study, to question "vaginal delivery is a natural and acceptable mode of delivery" those who responded yes were 155(67.3%) and those who responded no were 56(32.7%). From total no of participants who responded in this study, to question "seeing a baby immediately after vaginal delivery is a pleasure for mother" those who responded yes were 150(87.7%) and those who responded no were 19(11.1%) and those who responded don't know were 2(1.2%). To the question "in term of outcome, vaginal delivery is more pleasant" those who responded yes were 149(87.1%), those who responded no were 19(11.1%) and those who responded don't know were 3(1.8%). Total number of participants who responded about the question "vaginal deliveries create a more affectionate mother baby relationship" those who responded yes were 149(87.1%), those responded no were 20(11.7%) and those who responded don't know were 2(1.2%).

Table 2: Mode of delivery and knowledge of females about vaginal delivery

Descriptive analysis	Response (%)
Vagina delivery is natural and acceptable mode of delivery	
Yes	115 (67.3)
No	56 (32.7)
Seeing the baby immediately after vaginal delivery is a pleasure for mother	
Yes	150 (87.7)
No	19 (11.1)
don't know	2 (1.2)
The mother regains her health status soon after vaginal delivery	
Yes	151 (88.3)
No	20 (11.7)
In term of outcome, vaginal delivery is more pleasant	
Yes	149 (87.1)
No	19 (11.1)
don't know	3 (1.8)
Vaginal deliveries create a more affectionate mother baby relationsh	
Yes	149 (87.1)
No	20 (11.7)
don't know	2 (1.2)

Table 3 shows that from total number of participants who responded to the question "the emotional relationship

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between mother and baby after vaginal delivery is better" those who responded yes were 151(88.3%), those who responded no were 15(8.8%) and those who responded don't know were 5(2.9%). Who responded about the question "Vaginal delivery is less risky for mother" those who responded yes were 147(86.0%), those who responded no were 15(8.8%) and those who responded don't know were 9(5.3%). To the question "Vaginal delivery is better in long term" those who responded yes were 139(81.3%), those who responded no were15(8.8%) and those who responded don't know were 17(9.9%).

Table 3: Benefits of vaginal delivery (n = 171)

Descriptive analysis	Response (%)
The emotional relationship between mother and baby after vaginal delivery is better	
Yes	151 (88.3)
No	15 (8.8)
don't know	5 (2.9)
Vaginal delivery is less risky for mother	
Yes	147 (86.0)
No	15 (8.8)
don't know	9 (5.3)
Vaginal delivery is better in long term	
Yes	139 (81.3)
No	15 (8.8)
don't know	17 (9.9)

DISCUSSION

World Health Organization (WHO) recommendations to limit population-based caesarean section (CS) rates to 10–15 are linked to reductions in maternal, neonatal, and child mortality; however, the number of cases reaching robotic labor has increased over the last three decades [9]. This rise in CS rates creates a pressure on public health resources, particularly when CS is done needlessly, resulting in profit and service shortages, as well as worse mother and child health outcomes. There is more evidence that CS increases the likelihood of complications such infection, urinary tract infection, pain, headaches, anaesthetic issues, maternal mortality, and postpartum depression as compared to vaginal birth [10-12]. In this descriptive research, we surveyed primiparous women to see how much they knew about the various options for giving birth. An instrument for gauging primiparous mothers' familiarity with the various birthing options has been adapted for use with expectant women. In our study, more than 82% females had good knowledge about vaginal delivery and more than 80% females also know about benefits of successful vaginal delivery. In another Pakistan study, 68.1% of working women were thinking that those who want only one or two children are better to choose CS while 46.9% of housewives were in favor of CS in this regard. About 71.1% of working women and 43.1% of housewives were in favor of CS however 20.8% of working women and 40.2% of housewives were in favor of vaginal delivery [13]. The majority of Saudi Arabians (45.4%) scored poorly on a test measuring awareness of complications associated with having a caesarean section, while just 12.6% scored well [14]. Eighty-nine percent of the women surveyed in an Indian research had a favorable opinion of vaginal birth. Patients with primary and secondary infertility had a higher prevalence of caesarean sections because they believed their infants would be healthier if they were born by caesarean section rather than vaginally [15]. A research among 245 women in Nigeria found that only 68.6% of the women knew about non-pharmacological techniques of reducing pain in labor, and the vast majority of these women thought their knowledge was too trivial to put into practice [16]. An estimated 90% of Nepali moms who visited the antenatal OPD had at least a moderate understanding of the benefits and risks associated with each possible delivery method. The majority of women (93%) are supportive of having a vaginal birth, whereas 6.6% are not. Attitudes towards caesarean sections were generally good among 24%, negative among 75%, and neutral among the remaining 25% [17]. Decisions made in the context of clinical practice that have been decided and People may now make more informed choices about their health thanks to personalized treatment alerts. Voluntary CS rates were shown to be lower when women knew more about the procedures' prerequisites and potential problems [18]. The study's findings suggest that most pregnant women may be unaware of the possible health risks associated with different types of childbirth. Pregnant teens and mothers who had their previous kid by caesarean section were more likely to be ill-equipped to handle the information. The trimester of pregnancy makes no difference in terms of knowledge. Ten percent of expectant mothers in the most current survey preferred a caesarean section, and this preference was particularly strong among women who were older, employed, had many children, or had previously given birth through CS. The World Health Organization (WHO) has addressed the rising prevalence of CS in both developed and underdeveloped countries [19]. Jadoon *et al.*, demonstrated that sociocultural and institutional factors rather than national economic conditions are what drive the practice of CS [20]. Pregnant women who lack sufficient information may accept the doctors' advice without exploring potential alternative delivery options or comprehending the dangers of CS delivery [21]. Pregnant women's positive attitudes towards vaginal birth are increased when they are given accurate information about all of their birthing options [22]. In the Islamabad, 30.2 of the women who took the community-based test succeeded. In the region, there are

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few researches examining their demographic and artistic as obstetric concerns including mode of birth [23]. Not enough research has been done in Pakistan to determine the optimal method of CS delivery or the variables that influence women's and interpreters' choices to employ CS [24]. Women's knowledge of delivery options in Pakistan has to be investigated so that evidence-based policies and recommendations may be created to perhaps reduce the overall CS rate in the nation. Improved maternal education regarding the potential short- and long-term health problems associated with CS, especially repeated CS, should be a focus of efforts to minimize the incidence of CS, the research found. It is also important to make concerted attempts to include ANC appointments into which the possible benefits and drawbacks associated with different delivery methods are openly discussed. The findings of this study are congruent with those of earlier research [25].

CONCLUSIONS

The results of this research highlight the need to educate pregnant women on the health risks connected with each delivery option. About ten percent of expecting mothers choose caesarean sections. Health policy reform aimed at empowering women should be innovative and should include information about other options for childbirth.

Authors Contribution

Conceptualization: IZ
Methodology: HS
Formal analysis: RJ
Writing-review and editing: IZ, HS, RJ

All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

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Original Article

Assessment of Test Anxiety and its Correlation with Academic Performance among Undergraduate Students

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ABSTRACT

Globally, around one in every three medical students suffer from anxiety. Test anxiety is a physical, mental and emotional reaction to threat of failure in exams and consists of worry and perception as components and it may lead to poor academic performance. **Objective:** To assess the level of test anxiety and its correlation with academic performance among undergraduate students. **Methods:** This cross-sectional analytical study was conducted from 1st September to 15th December, 2022 with purposive sampling technique to collect the data from the undergraduate students at Sohail University, Karachi. Westside Test Anxiety Scale questionnaire was used. Data were analyzed by using SPSS version-22.0. Descriptive statistics, Mann Whitney and Spearman's correlation were measured. **Results:** 44% of the participants were male, 94% were single, 50% were nursing students and 57.5% were 1st and 2nd year undergraduate students. Majority of the respondents (70.5%) were suffering from high to extremely high-test anxiety whereas (17.5 %) participants had mild to moderate level of anxiety. The significant association was found between test anxiety and study program (p-value 0.021). The weak reciprocal correlation coefficient was found between academic performance and test anxiety (r = -.473). **Conclusions:** Findings of this study suggest that 88% of undergraduates had high to extremely high-test anxiety. A significant link between the study program and level of anxiety and a significant correlation were also found between academic performance and test anxiety. The causes and contributing elements of anxiety must be addressed. The test anxiety puts the undergraduates on high risk for learning deficits and unhealthy consequences.

INTRODUCTION

Anxiety is an emotion which consist feelings of tension, physical changes and worried thoughts. In addition, anxiety disorders are the most common type of mental health diseases with approximately 15% lifetime incidence. Poor health can be caused by anxiety, and students feel during their examinations [1]. Test anxiety which is a physical, mental and emotional reaction to risk of failure in exams and consist of worry and perception as components. Both, worry and perception have an impact on students' academics, interpersonal relations, self-confidence and mental health [2]. Exam anxiety influence student's academic achievement, their mental and physical wellbeing thus resulting in a low quality of life [3]. Because, the students with high levels of anxiety have a low success. Moreover, extreme level of worry is dangerous for physical and psychological health and affects a person's ability to perform his personal, social, familial, professional, and academic actions [4]. Among the students of health profession, 25% to 65% are suffering from test anxiety [5]. This test anxiety affects their motivation, focus, learning, performance in exams, and even cause them to drop out of university [5]. Globally, approximately one in every three undergraduate medical students suffers from anxiety, representing a 33.8% occurrence rate that is higher than the general population. Stress and anxiety also experienced by nursing and physiotherapy students [6].

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The undergraduate students may experience anxiety for a variety of reasons, including last-minute studying, lack of sleep, ineffective time management, and lack of confidence [7]. A previous study showed linked between test anxiety and low academic achievement as test anxiety is also related to psychological problems, parental pressure, irrational thoughts about tests, results etc. [8]. Students frequently struggle to adjust their academic life, which promotes the prevalence of depressed emotions which impact negatively due to worry and uncontrolled situation of exams [9]. Students with moderate test anxiety can concentrate more on the paper as compared to those with high levels of anxiety [10]. Test anxiety may increase due to poor memory and perceived level of stress among health sciences students. Specifically, in Pak-Indian subcontinent, the psychological distress has been increased among Pakistani (70%) and Indian students (49.1%) [11]. Test anxiety leads to worry which represents the decline in intellectual aspect of a learner and this intellectual aspect is associated with cognitive impairment, poor concentration and exam performance. So, the assessment of test anxiety is quite necessary [12]. This concern is considered valuable in multiple studies even in the context of Pakistan [1, 2] but mostly the attention paid to general students and less attention has been paid undergraduate health sector students. No previous study in the public or private sector in Pakistan was found regarding the prevalence of test anxiety and its correlation with academic performance among undergraduate health sector students. Therefore, this study was aimed to assess the level of test anxiety and its correlation with academic performance among undergraduate health care students in Karachi.

METHODS

This cross-sectional analytical study was performed from 1st September to 15th December, 2022 including 200 willing undergraduate students at Jinnah College of Nursing, Jinnah College of Rehabilitation and Jinnah College of Pharmacy, Sohail University Karachi. The students of post-graduation, specialization and other disciplines and who were unwilling were excluded from this study. For sampling, purposive sampling technique was used. By using Slovin's formula i.e. $n = N / (1 + Ne^{\wedge 2})$ where n is the sample size, N is population (400), and e is the margin of error (0.05) and 95% level of confidence, we estimated the sample size which was 200 [13]. Data were collected through a self-developed demographic form. Moreover, Westside Test Anxiety Scale (WTAS) was used which consist of 10 questions on self-assessment of anxiety and cognitive impairment. Westside test anxiety scale is a valid technique of assessing test anxiety of r = 0.44 with WTAS score; positive score indicates improved performance in those with lower levels of test anxiety. The test comprises 6 questions on dealing with memory loss and impaired cognitive processing, as well as 4 questions about exam anxiety. The response was given a score between 1 and 5, with scores more than 3 suggesting intervention needs and abnormally high-test anxiety. The WTAS questionnaire scores were categorized into low, normal or average, high normal, moderately high, high and extremely high-test anxiety levels; as per standard recommendations [12]. An ethical approval was taken from Ethical Review Committee Sohail University, Karachi (ERC-Protocol #:000234/22). Permission for data collection was obtained from head of all three departments. Informed consent form was given to the participants before filling questionnaire. The academic performance of respondents was assessed by their relevant department and we took from them. Data were analyzed by using SPSS version-22. Descriptive statistics, Mann Whitney and Spearman's correlation were used for frequency, percentages and correlation values. P-value ≤ 0.05 was considered as significant.

RESULTS

Out of 200 respondents 88 (44%) were male, 103 (51.5%) students were in between of 17-21years of age, 12 (6%) participants were married, 100 (50%) of the students were from nursing department and 115 (57.5%) undergraduates were studying in 1st and 2nd year (Table 1).

Table 1: Demographic Characteristics of Study Participants (n=200)

Age	17-21years	103(51.5%)
	22-26years	97 (48.5%)
Sex	Male	88 (44%)
	Female	112 (56%)
Program	G-BSN	100(50%)
	Pharm-D	50 (25%)
	DPT	50 (25%)
Year of Study	1st & 2nd year	115(57.5%)
	3rd & 4th year	85(42.5%)
Marital Status	Married	12 (6%)
	Unmarried	188 (94%)

Table 2 shows the percentage and frequency of test anxiety score. Out of 200 participants, Majority of the individuals 141 (70.5%) were suffering from high test anxiety to extremely high-test anxiety whereas 17.5 % (n=35) partakers had mile to moderate level of anxiety. Moreover, and only 12 % (n=24) were found normal on anxiety score.

Table 2: Percentage and Frequency of test anxiety score (n=200)

Test Anxiety Scale	Score	Frequency (%)
Comfortably low-test anxiety	(1.0–1.9)	10(5)
Normal or average test anxiety	(2.0–2.5)	14(7)
Mild test anxiety	(2.5–2.9)	8(4)
Moderately high (some items rated 4=high)	(3.0–3.4)	27(13.5)

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High test anxiety (half or more of the items rated 4=high)	(3.5–3.9)	47(23.5)
Extremely high anxiety (items rated 4=high and 5=extreme)	(4.0–5.0)	94(47)
Total Population	-	200(100)

Table 3 shows the correlations of test anxiety with demographic data. In which the Mean Rank of age group 1, male, married, year 1 & 2 and Pharm-D students were high (93.94, 94.31, 95.63, 98.47, 111.36 respectively) with the P-value (0.895, 0.805, 0.191, 0.132 and 0.021 respectively). The only significant result was found between test anxiety and study program (p-value 0.021).

Table 3: Correlations of Test Anxiety with demographic data (n=200)

Variables	Categories	Mean Rank	p-value
Age	17 to 21 years	93.94	0.895
	22 to 26 years	93.03	
Sex	Male	94.31	0.805
	Female	92.63	
Marital Status	Married	95.63	0.191
	Un-married	91.23	
Study Year	1st & 2nd Year	98.47	0.132
	3rd & 4th Year	88.20	
Study Program	Generic BSN	103.40	0.021
	Pharm-D	111.36	
	DPT	83.84	

Table 4 shows the correlation between test anxiety and academic performance. The significant correlation coefficient was found between academic performance and test anxiety (P-value <0.0001). There is an inverse weak correlation between anxiety score and academic achievement, as anxiety score up to 1 degree will lead to academic performance by 0-.473.

Table 4: Correlation between Test Anxiety and Academic Performance (n=200)

Correlations			Test Anxiety Score	Test Percentage
Spearman's rho	Test Percentage	Correlation Coefficient	1.000	-.473**
		Sig. (2-tailed)	-	<0.0001
		N	200	200
	Test Anxiety Score	Correlation Coefficient	-.473**	1.000
		Sig. (2-tailed)	<0.0001	-
		N	200	200
Correlation is significant at the 0.01 level (2-tailed)				

DISCUSSION

The findings of the study revealed that more than ¾ of the students had high to extremely high-test anxiety. These results are similar to study by Macauley *et al.*, [1], which found greater than normal anxiety among their participants. Contradictory results were found that partakers had moderately highly anxiety in a previous study that was conducted in 2018 in Pakistan [2]. Some other studies also support these findings and report highest anxiety levels among the students [4, 14, 15, 16]. Contrarily, moderate level of test anxiety revealed in numerous studies [17-19]. A past study reported mild anxiety level among his undergraduate participants [18]. The significant prevalence of anxiety was also observed by Shafique in her study during the year 2020 [3]. The possible causes for this increased prevalence of anxiety among students may be parental expectations, extensive course content, less facilitation by teachers, institute culture and peer pressure [1-3]. While observing the Mean Rank of demographic variables and their correlation with test anxiety, the significant association was retrieved only in study program. The students of Pharm-D program had high test anxiety (111.36 on Mean Rank). Similarly, these results were also found in a past study in which Pharm-D students had increase level of test anxiety [8]. On the other hand, Desai *et al.*, observed higher anxiety levels in physiotherapy pupils [7]. Anxiety levels were also found higher among MBBS students reported a former research conducted in 2017 [13]. The researchers stated that academic burden, difficult course content, maladjustment in novel environment are the influential factors that causes anxiety and stress among health profession undergraduates [7, 13]. Test anxiety was found high among our male students (94.31 on Mean Rank) without significant correlation of gender with test anxiety similar to a past study [14]. Although it is revealed in few past studies that prevalence of test anxiety is much higher among female undergraduates [6, 8, 9, 15, 16]. This higher anxiety may be prevailing due to less opportunities, social and cultural restraints, family issues and instability in novel environment for girls. The current study observed high levels of anxiety among 1st and 2nd year students instead of 3rd and 4th year undergraduates. Similar results were found in a past research [8]. Duraku *et al.*, in 2017 found highest anxiety levels among 1st year students [17]. Contrarily, some researchers found high levels of test anxiety among their senior students [4, 16]. We may suggest that with the passage of time, students increase their self-confidence, develop learning skills and competencies and it may lead to decrease in undergraduates' anxiety level. This study observed inverse correlation between test anxiety and academic performance as anxiety score increase up to 1 degree the academic achievement will decrease to 0-.473. It shows that high level of anxiety interferes students' motivation, learning and academic achievement [5]. Balogun *et al.*, denoted that undergraduates with high level of test anxiety are likely to forget what they read. These results were also supported by numerous previous studies [5, 8, 10, 16, 17]. On the contrast, Brady *et al.*, in his study

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which was conducted in 2018 affirmed that those students who were less certain regarding their exam performance due to greater anxiety got benefit from the reassessment of their contributing factors showed decreased anxiety and improved academic performance in the examinations [19]. The undergraduate students should also take help from their supervisors, mentors and teachers to relieve their anxiety. Meanwhile, on clinical site, preceptors should pay attention to deal psychological needs of nursing s undergraduates during their tenure and provide psychological training to undergraduates like positive meditation, music therapy, spiritual help, breathing training, aromatherapy and guided refection [20]. University personnel should be incorporating psychological management training during initial semesters [21]. Cipra and Müller-Hilke *et al.*, suggest that medical personnel place precise emphasis on applying strategies for coping with anxiety and effective learning [22]. The faculty members and mentors can support their undergraduates in lessening test anxiety, and they also need to know how to help nursing students to develop strengths and coping mechanism to overcome test anxiety. Involvement of parents/guardians can also help to manage psychological problems and test anxiety.

CONCLUSIONS

The current study emphasizes the level of test anxiety among undergraduate students and observed its correlation with their academic performance. The findings of the study revealed that majority of the undergraduates had high to extremely high-test anxiety. A significant link between the study program and anxiety were also found. The significant correlation coefficient was found between academic performance and test anxiety. There is an inverse weak correlation between anxiety score and academic achievement, as anxiety score up to 1 degree will lead to academic performance by 0-.473. The test anxiety puts the undergraduates on high risk for learning deficits and unhealthy consequences.

Authors Contribution

Conceptualization: KH
Methodology: SK, KH, MS, G, T, IT
Formal analysis: TA, AA
Writing-review and editing: KH, TA, AA

All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

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Original Article

Prevalence of Insomnia in Menopausal Women

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ABSTRACT

Menopause represents a pivotal period in a women's life, encompassing significant biological, psychological, and social transformations. The majority of women going through menopause commonly encounter the challenge of experiencing recurring and frequent insomnia. **Objective:** To determine the prevalence of insomnia in menopausal women in Rawalpindi and Islamabad. **Methods:** Between November 2022 and June 2023, following the duration of 6 months, a descriptive cross-sectional investigation was undertaken, involving 267 menopausal women. The data were gathered from the general population of Rawalpindi/Islamabad, encompassing both housewives and hospital outpatients, utilizing a convenience sampling. Those individuals fulfilling the eligibility criteria underwent evaluation for insomnia employing the Athens Insomnia Scale. Data analysis were conducted utilizing SPSS version-25. **Results:** Out of 267 participants, 43.1% had insomnia when assessed by AIS-8. The mean age of the participants was 51.80 ± 7.197, onset of menopause was < 5 years by majority (70.8%) of the females with the most prevalent symptom of insomnia, "Final awakening earlier than desired" while the least common was "Impairment in functioning during the day" reported by menopausal women. **Conclusions:** Our study findings indicated that insomnia is prevalent among menopausal women, with the most common symptom being waking up earlier than desired. On the other hand, the least commonly reported symptom among menopausal women was impaired daytime functioning due to insomnia.

INTRODUCTION

Sleep is defined by diminished motor movements, lowered stimulus response, standardized posture, and very simple reversibility process [1]. The act of sleeping is not a uniform process. It comprises two distinct categories: REM sleep, which stands for rapid eye movement sleep, and NREM sleep, which stands for non-rapid eye movement sleep. These two categories exhibit fundamental differences. Both the circadian and homeostatic processes are involved in regulating sleep [2]. There is strong relationship between sleep duration and various health indicators. However, the adverse effects of inadequate sleep appear to hold a substantially greater significance in contemporary society [3]. Sleep needs refer to one's typical sleep duration when not influenced by previous sleep deficits, while inadequate sleep is defined as a level of sleepiness that begins to lead to cognitive and functional impairments [4]. Inadequate sleep has adverse effects on cognitive functioning, mood regulation, and recovery after physical activity. Additionally, compromised sleep quality can detrimentally influence decision-making, the speed and accuracy of task performance, as well as recovery following exercise. Factors such as age, psychological and physiological conditions, cultural influences, and environmental elements collectively influence both the quantity and quality of sleep we experience [5]. Females are more likely than males to report experiencing insomnia

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[6, 7]. Insomnia is defined as, lack of satisfaction with either the quality or quantity of sleep. This is frequently accompanied by trouble falling asleep, trouble staying asleep, frequent awakenings or trouble falling back to sleep following awakenings, and early morning awakenings with difficulties falling back to sleep. The disturbance occurs at least three evenings a week for 1 to 3 months [8]. Notable proportion of women face sleep difficulties as they approach and navigate through menopause [9]. Around 26% of these women experience severe symptoms that disrupt their daily functioning and potentially expose them to the risk of being diagnosed with insomnia. Annually, the menopause transition impacts over 500 million women aged between 42 and 55, with an average age of 51 [10]. Menopause is characterized by the cessation of ovarian follicular activity resulting from a decline in estrogen levels. An indicator of menopause is the cessation of menstrual flow for a minimum duration of one year [11]. The menopausal transition unfolds progressively and encompasses three distinct stages with evident clinical manifestations: premenopausal, perimenopausal, and postmenopausal. Premenopausal individuals were identified as those who experienced consistent and regular menstrual cycles over the preceding 12 months and were at least 35 years old. Perimenopausal individuals were characterized by irregular or absent periods for a duration of three to twelve consecutive months. Postmenopausal individuals were those who affirmed that their last menstrual period occurred more than a year ago [12, 13]. Sleep problems, such as increase insomnia, reduced sleep quality, and increased sleep disruptions, are commonly observed in peri- and postmenopausal women. Notably, a robust link exists between insomnia and coronary heart disease (CHD), particularly in the context of postmenopausal women [14]. While the majority of symptoms experienced during menopause are not fatal, they do exert a negative impact on the social and professional aspects of middle-aged women's lives, as well as their overall quality of life [15]. The number of women experiencing menopause is increasing day by day as due to their increasing age and certain other external factors. Health care centers now have separate departments for middle-aged women because chances of having comorbidity increases with the age and menopause. Although the prevalence of insomnia and association of insomnia with menopause have been well reported internationally, but limited work has been conducted on insomnia and menopause in Pakistan. The objective of the present study was to determine the prevalence of insomnia among menopausal women in Rawalpindi/Islamabad, Pakistan.

METHODS

A descriptive cross-sectional study was conducted on 267 menopausal women aged above 35 who had been in a state of menopause for at least a year. The data were collected from general population of Rawalpindi/Islamabad (including house wives and hospital OPD patients) through convenient sampling on the duration of 6 months from November 2022 to June 2023.Participants with any psychiatric disorder, cardiac problem, asthma, overactive thyroid, hysterectomy, history of polycystic ovarian syndrome, history of sleep issue before menopause, being on sedatives or hypnotic drugs, were omitted from the study. After obtaining informed consent, self-structured questionnaire was used to collect information regarding demographics of the menopausal women. Participants who met inclusion criteria were assessed for insomnia by Athens Insomnia Scale (AIS-8). The AIS-8, is an 8-item self-report questionnaire with high internal consistency, a Cronbach's alpha of 0.89 that measured the intensity of sleep difficulties. Five items out of 8 assessed difficulty in sleep induction, awakening during the night, early morning awakening, total sleep duration, and overall sleep quality. Remaining three items pertained to the next-day consequences of insomnia (sense of well-being during the day, functioning (physical and mental) during the day, and sleepiness during the day). A 4-point numeric rating system is used to provide ratings for each item, with 0 denoting no problems at all and 3 denoting highly serious issues. AIS-8 has a total score range of 0 to 24. Insomnia is deemed to be present when a score of 6 or higher is obtained [16]. The sample size was calculated using Rao Soft Software. With population estimate of 20,000, sample size of 267 was recommended by the software. The margin of error was 5%, the confidence level was 90% and the response distribution was 50%. All the work was done after the approval from ethical review committee of Margalla Institute of Health Sciences, Rawalpindi (Ref. No. DK/176/22, dated November 11, 2022). Data were gathered after written consent from the participants. Participants had their right to ask any question regarding study or to terminate their participation at any point. Descriptive statistics were used to examine the data collected through questionnaires (e.g., mean and standard deviation). Data were presented in graphical and tabular form. All the statistical analysis were conducted using SPSS 25 software(SPSS Inc. Chicago IL, USA).

RESULTS

Questionnaires were distributed among 303 participants, out of which 35 did not fulfil the eligibility criteria were excluded from the study. Out of the remaining 268 participants, 1 was not willing to give data, final data were analyzed for 267 participants. Demographic details of participants were recorded, and each participant was

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interviewed individually in order to complete the data. The mean age was 51.80 ± 7.197 years, mean height was 163.17± 10.495cm, mean weight of the participants was 77.91 ± 11.106kg, and mean BMI turned out to be 29.67 ± 6.004 as shown in table 1.

Table 1: Demographics

Variables	Mean ± SD
Age (years)	51.80 ± 7.197
Weight (kg)	77.91 ± 11.106
Height (cm)	163.17± 10.495
BMI	29.67 ± 6.004

Table 2 shows the symptoms of insomnia as described by AIS-8 scale in percentages.

Table 2: Symptoms of Insomnia

Symptoms of Insomnia	Mean ± SD
Final awakening earlier than desired	57.7%
Sleep induction	56.9%
Awakening during the night	56.2%
Total sleep duration	53.2%
Sleepiness during the day	52.4%
Sense of well being	51%
Overall quality of sleep	49.8%
Functioning during the day	43.1%

Table 3 shows frequency and percentage of insomnia by using AIS-8. According to this scale 43.1% of menopausal women were having insomnia with a score of 6 or higher.

Table 3: Prevalence of Insomnia

Prevalence	N (%)
Insomnia (≥6)	115 (43.1)
No Insomnia (<6)	152 (56.9)

DISCUSSION

The aim of the present study was to explore the prevalence of insomnia among menopausal women residing in Rawalpindi and Islamabad. The results illuminated a significant prevalence of insomnia within this demographic, affecting a notable 43.1% of the participants under investigation. This discovery sheds light on the pertinent issue of sleep disturbances during the menopausal phase. These findings were consistent with the work done by Wang *et al.*, and Arakane *et al.*, [15, 17]. The findings of current diverged from the research conducted by Monterrose *et al.*, [18], which indicated a 27.5% prevalence of insomnia among females. This variance could potentially be attributed to differences in age distribution. The present study included a larger proportion of females aged 50 and above. Previous literature suggests a correlation between age and increased insomnia rates, and it's noteworthy that the prior study encompassed various menopausal stages, whereas our investigation specifically focused on postmenopausal women. In a different investigation carried out by Shan *et al.*, a prevalence of 59.6% was recorded for insomnia among females [19]. The rise in insomnia occurrence, when contrasted with present study, can be attributed to variations in age demographics. Previous study included females aged 40 to 89 years, which contributes to the disparity in insomnia prevalence. Rahman *et al.*, Conducted an additional study that concluded dissimilar outcomes compared to the present research, indicating a prevalence of 52.2% [20]. This variance can be attributed to the fact that the former study comprehensively assessed all menopausal symptoms, encompassing sleep disorders, utilizing the MRS tool. In contrast, our study specifically focused on the aspect of insomnia.

CONCLUSIONS

Our study findings indicated that insomnia is prevalent among menopausal women, with the most common symptom being waking up earlier than desired. On the other hand, the least commonly reported symptom among menopausal women was impaired daytime functioning due to insomnia.

Authors Contribution

Conceptualization: KB, UK, FA, HK, SM, RB
Methodology: SM, RB
Formal Analysis: KB
Writing-review and editing: KB, UK, FA, HK, SM, RB

All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

The authors declare no conflict of interest.

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Original Article

Compare the Effectiveness of Mulligan (Nags & Snags) and McKenzie (Self-Stretching) On Improving the Pain and Functional Ability in Patient with Chronic Neck Pain

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ABSTRACT

Neck pain is Consider the major problems and the prevalence of this musculoskeletal disorders are very common in people. **Objective:** To compare the effectiveness of mulligan and McKenzie on improving pain and functional ability in chronic neck patient. **Methods:** This trial was registered with Iranian trail registry with reference no: IRCT20220414054537N4. It's a Double-Blind Randomized Clinical Trial that was conducted in DHQ Hospital Shadrah a affiliated teaching hospital attached with Afro-Asia University Lahore from 1 May 2022 to 30 June 2022.The sample size was calculated and total 26 patients were divided into two groups. The ages of the patients were around 20-55 years old. The entire patient having the mechanical neck pain was included in this study. Patients were selected from DHQ hospital in May to June 2022 duration. In group A we applied the mulligan technique of manual therapy treatment that included the Natural apophyseal glides, sustained natural apophyseal glides and Self SNAGs in sitting position of the patient. The second group of 13 patients had applied the Mackenzie exercises in seven motions like 4 movement of neck extension,2 movements in lateral flexion and rotation and one movement in flexion direction. **Results:** Overall the post Numeric pain rating scale and Neck Disability index was significantly improved in group A which received the NAGs & SNAGs Mobilization technique. **Conclusions:** Mulligan (NAGs SNAGS) is effective than Mackenzie (self-stretching) treatment technique to improve the functional ability and reducing pain in chronic neck patient.

INTRODUCTION

Neck pain is Consider the major problems and the prevalence of this musculoskeletal disorders are very common in people. Due to technology and differential professional job role it is considered that a lot of people spend their maximum time in sitting position now a days at work It is estimated that out of 3 ,1 person is affected by this neck problem now a day's specifically in middle age [1]. Total burden of the neck pain was calculated by available statistics, and it was concluded that it ranks among the 4th position in worldwide disease 4th highest in terms of disability as measured by years lived with disability (YLD), and 21st in terms of overall burden. Cervical pain that is originated from mechanical in nature relatively different from the pain due to anatomical and structural cause. Patient with mechanical neck pain or chronic neck pain having no specific reason in disturbance of structure like

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capsular, cartilaginous and ligament level. There are many factors that lead to the symptom chronicity that included poor body positioning during work that apply more stress on the body, psychological stress, Sports related activity and Occupational related task. Pain in the neck area can be take place at the any level from First thoracic spine inferiorly toward nuchal line superiorly and till the lateral level of the neck [2]. It is the second most occurring musculoskeletal problem after Low back pain. The prevalence of the neck pain in most recent research show the result range from 43-66.7% and the age is the major factor that cause the neck pain. The nature of the pain is wide ranged and it different in different musculoskeletal condition it may be traumatic, recurrent and it may be persistence [3]. Major reason of developing neck pain due to the Disc related pathologies like heriation, buldge, sequestration, Radiating pain of the cervical, and the myofascial pain syndrome. Neck pain may be initiated due to muscle strain or due to maintaining any abnormal body posture and using poor ergonomics environment in their workplace. Sometimes this pain may go away in 1-3 weeks or sometimes it takes much longer duration and become chronic [4]. The result of a met analysis also showed some concern that these manipulations put some extra stress on the soft tissue and leads to the injury so mobilization simple is quite safe as compare with the manipulation [5]. The concept of Mulligan's is based on the Kaltenborn principle for recovering and restoring accessory physiological joint movement [6]. By applying a parallel force to the facet joint of spine it helped to mobilize the spinal joint in weight bearing position by using the concept of Kaltenborn [7]. The mulligan technique expressed as passive oscillatory treatment process that apply the parallel force on the facet joint planes of the cervical, upper thoracic spine. Both NAGs and SNAGs considered best treatment protocol in increasing the range of motion, reducing the pain intensity, and improving the neck functional mobility in patients with cervical radiculopathy [8]. Mackenzie exercise, stretching exercises and traction therapy are being applied in clinical practice [9]. In particular, the Mackenzie exercise is one of the self-stretching exercises. Posture correction by relaxing the tense muscles by the patient himself. As an effective intervention method to improve neck alignment [10]. The forward head posture causes the superficial muscles to exert excessive muscle activity and because it supports the head in the wrong posture together, daily life You will experience discomfort during your life. These symptoms in order to treat it, various interventions have been methods have been reported so far. Therefore, the patient is actively Self-stretching exercise mediated by a therapist and a therapist or machine Manual stretching exercise for 4 weeks to intervene in anterior head posture Muscle activity and neck alignment in patients with chronic neck pain accompanied by Analyze the factors affecting the function and verify the effect related to functional recovery and to provide clinical basic data for this [11]. Our focus in this study was to analyze the best way to treat the neck pain due to abnormal posture of the neck. The aim of the study to understand the effectiveness of the SNAGs versus self-stretching.

METHODS

This is double-blind randomized controlled trial. This trial was registered with Iranian trail registry with reference no: IRCT20220414054537N4. The sample size was calculated by the mean value of the referenced article using the epitool method for sample size calculation and total 26 patients were divided into two groups [12]. The ages of the patients were around 20-55 years old. The entire patient having the mechanical neck pain and pain due abnormal posture of neck like forward head posture were included in this study. Patients were selected from DHQ hospital in May to June 2022 duration. All the patients that were Included for the study should base on Biondi questionnaire [13]. All the patients should have greater than 20% neck disability index score and the score of Numeric pain rating will be more than 2-3 points. All participants were excluded from this study if they had any hearing problem, vision disorder, smell issues or any kind of taste related problem. All participant those were having any systematic problems, like tension headache, Rheumatic arthritis, several viral and bacterial infection, Inflammatory disease, migraine, any neurological problem, and fracture in neck region were excluded from this study [12, 14]. The examiner of the study was also blind. The consent form from the patient were taken at the start of the study and patient after reading the form showed their availability and consent for this trail study [12]. The Experimental group applied with the mulligan technique of manual therapy treatment that included the Natural apophyseal glides, sustained natural apophysial glides and Self SNAGs in sitting position of the patient. NAGs movements are the oscillatory Movement and these mobilizations tend to be provided in anterio-cranially direction of the selected cervical joint. The movement of the force is in parallel direction toward the restricted cervical facet joints. We have applied 3 sets of 6 repetitions each and the intensity of dosage was maintained in 2-3 hertz. The procedure of the movement as per the following instruction of the mulligan in which we had applied the sustained glide and asked the patient to move its neck in several direction like Flexion, Extension, Side flexion and rotation and these movement was maintained in pain free direction and range [15]. The second group of 13 patients with chronic neck pain was

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given the following treatment strategies in which we had applied the Mackenzie exercises in seven motions like 4 movement of neck extension,2 movements in lateral flexion and rotation and one movement in flexion direction. The pre and post value was monitored by performing the Mackenzie technique in the patient and its effect on the body was also monitored as well especially in soft tissue area of the neck in the body. Both sides of the body were measured and compared with each other. The time to take the new reading is 10 second. The Body skin of the neck area was pushed by 0.18 N force and after the pre-load a force of 0.58N was applied to the neck skin at the interval of 15 ms. Thereafter, the vibration on the skin surface was triggered by Myoton PRO (Myoton AS, Estonia), a muscle tone measurer, which was used to examine the bio mechanic indices [16,17]. The Numeric pain rating scale and Neck disability Index as an outcome measuring tools. Statistical analysis was performed to analyze the effect of the treatment applied to the subjects of both control and experimental groups. It was done by using the IBM SPSS Inc.25.0 version. For this, the data were incorporated in MS excels spreadsheet. Out of 26 subjects 13 were randomized into Group 1 and 13 are randomized into Group 2. All the 26 subjects complete the entire protocol as defined by 2 months of treatment and pre and post value were taken by using the Numeric pain rating scale and Neck disability scale. The outcomes of the study were neck pain and Functional Ability. The following treatment applies with the frequency of 4 times a week and the whole treatment session was continued for 8 weeks. Total 32 sessions were given to both groups and the follow-up were taken after the 8 weeks and evaluated after this. Statistical tools were applied, and data were normally distributed to between group comparison calculated by paired t-test and for the in between groups and independent sample t-test for between both groups post value. Descriptive measures like mean, the standard deviation was reported along with the p-value.

RESULTS

The study was conducted on 26 subjects. The diagnose Chronic Neck Pain from both genders included in this study. Overall, 26 populations were divided into two groups of 13,13. Out of 26 patient 16 were the male patient and 10 were the female. Out of 26 the 6 patients where BMI underweight and 20 were containing the normal BMI. All the subjects were a mean age of 25.27± 3.29 of experimental group and conventional group. Mean and standard deviation of BMI for experimental group and for conventional group was 1.77 ±0.43. Table 1 Showed the mean and standard deviation of Numeric pain value in Experimental group and control in between group (independent sample t test value).The mean and standard deviation of Numeric Pain rating scale in pre value in group A was 7.38± 0.65 and Group B was this7.46±0.8. The post value of Numeric pain rating scale in group A was 1.07±0.64 and in group B was this4.00±1.08. The mean difference between pre and post Numeric pain rating scale value in group A was calculated 6.31±0.01and group B was3.46±-0.21. The p value between pre and post value within group (<0.05)show significant difference.

Table 1: Showed the mean and standard deviation of Numeric pain value in Experimental group and control in between group (independent sample t test value)

Numeric Pain Rating scale	Experimental Group	Control Group	p-value
Pre-Numeric Pain rating scale	7.38±0.65	7.46±0.87	0.802
Post Numeric Pain rating scale	1.07±0.64	4.00±1.08	0.000
Mean Difference	6.31±0.01	3.46±-0.21	

Table 2 Showed the mean and standard deviation of neck disability index in Experimental group and control in between group(independent sample t test value)The mean and standard deviation of Neck Disability scale in pre value in group A was 7.38±0.65 and Group B was7.46±0.87 the post value of Neck Disability scale group A was 1.07±0.64 group B was7.46±0.87. The mean difference between pre and post Neck Disability scale value in group A was 6.31±0.01 and group B was 3.46±-0.21. The p value between pre and post value within group (<0.05) show significant difference.

Table 2: Showed the mean and standard deviation of neck disability index in Experimental group and control in between group(independent sample t test value.

Neck Disability Index	Experimental Group	Control Group	p-value
Pre Neck-Disability Index	37.15±4.23	36.84±3.80	0.847
Post Neck Disability Index	13.53±6.32	23.69±7.50	0.001
Mean Difference	23.62± -2.09	13.15± -3.70	

DISCUSSION

There was no significant difference between the pre-treatment values of two groups according to numeric pain rating scale and neck disability index (p value <0.05) Overall the post Numeric pain rating scale and Neck Disability index was significantly improved in group A which received the NAGs & SNAGs Mobilization technique. The p value while comparing the post value of group A and group B was significant. The Overall post Numeric rating scale and disability index values improved in both groups and the p value had been significant. It had observed that significant improvement had seen because the p value was significant while comparing the post value in Numeric Pain rating and neck disability index of both groups A and B. The result of our study has shown the improvement in the neck disability score and pain scale but when we compare the effect it has showed that SNAGs has given better result as compared to

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the mulligan techniques. But in group A Both the Pain scale and the neck disability in chronic neck pain showed the improvement in the symptoms and other Activities by applying the mulligan techniques these result has given the same result as we received in some previous result by Ali *et al.*, They concluded that Patient with chronic neck pain has given the better outcomes and improvement in the neck disability scale and pain scale by Applying The NAGS & SNAGs [18]. The result of our study has shown the improvement in the neck disability score and pain scale but when we compare the effect it has showed that SNAGs has given better result as compared to the mulligan techniques. Our study result is coherent with the result we received by the study of Lopez *et al.*, He Concluded that SNAGs Showed better result as compare to other Manual therapy techniques [19], We have applied both SNAGs NAGs combined to received better outcomes in term of improving neck function, Range of motion, Pain and other neck related functional movement. In group A we have received the better significant outcomes in improving neck disability scale and pain scale. This study is coherent with the result of study conducted by Put *et al.*, The concluded the result in their study that Mulligan technique showed superior result in improving the Range of motion, pain and neck function as compared to the other group which received multimodal therapy which included the Massage in cervical spine area, Ultrasound and electrotherapy [20]. We have received the significant improvement in Group A in the neck function and improvement in all aspect of neck movement because when we calculated the result of both group A(Mulligan) and Group B(Mackenzie). This study is coherent because one of the study of few year back also has done the same procedure by applying Mulligan technique and Maitland technique to compare these techniques. They received that after applying the 1-month period of treatment in both groups Maitland and mulligan that NAGs & SNAGs showed the better clinically significant improvement as compared to the Maitland technique. Gautum concluded that Mulligan is better treatment protocol than other treatment techniques [21]. In group A Both the Pain scale and the neck disability in chronic neck pain showed the improvement in the symptoms and other Activities by applying the mulligan techniques these result has coherent with the Ahmad *et al.*, in 2013 concluded the same result after taking the measurement in pre and post value in both groups applying the mulligan and Kaltenborn. They found that after giving the mulligan techniques in patient with neck pain shoed the better result as compare to the Kaltenborn mobilization group [22]. There was no significant difference between the pre-treatment values of two groups according to numeric pain rating scale and neck disability index (p value <0.05). Overall the post Numeric pain rating scale and Neck Disability index was significantly improve in group A which received the NAGs & SNAGs Mobilization technique. The p value while comparing the post value of group A and group B was significant. The study result is coherent with the study of abdelgalil *et al.*, in which he concluded that mulligan with exercise showed better result but when we compare the Mulligan with exercise and without exercise this showed non-significant result. But as we have received the clue that both groups show same level of improvement hence, we found the significant improvement has seen in SNAGs & NAGs (Mulligan technique) [23]. The result of our study has shown the improvement in the neck disability score and pain scale but when we compare the effect it has showed that SNAGs have given better result as compared to the mulligan techniques. This study has given the same research base result we found in the study of El Sodany *et al.*, in 2014 in which he explained the application of mulligan techniques, exercises and mobilization with exercises and alone exercise. They concluded that SNAGs Group has given the better result as compared to the others group [24].

CONCLUSIONS

Mulligan (NAGs SNAGS) is effective than Mackenzie (self-stretching) treatment technique to improve the functional ability and reducing pain in chronic neck patient. Limitation of this research was low sample size and extensive scale that was unable to fill appropriate.

Authors Contribution

Conceptualization: SN, NJ
Methodology: SN, AJ
Formal Analysis: AI, AJ, TI
Writing-review and editing: SN, TI, FG

All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

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Original Article

Level of Knowledge of Bedside Nursing Staff Regarding Phlebitis of a Tertiary Care Hospital, Karachi

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ABSTRACT

Phlebitis is the inflammation of the vein's inner layer, venous tunica intima called phlebitis. The complications that commonly occur due to phlebitis are erythema, pain, swelling, and palpable thrombosis of the cannulated vein. **Objective:** To identify the current knowledge of bedside nursing staff regarding phlebitis. **Methods:** A cross-sectional study was carried out to find knowledge regarding phlebitis among nurses through self-administered questionnaires with 100 bedside nurses working in different wards of a Private Tertiary Hospital in Karachi, Pakistan, by a convenient sampling technique. Data were collected and analyzed by the SPSS software version-22. **Results:** The result of this study showed that among 100 participants, 50% participants have inadequate knowledge regarding phlebitis, 44% had average, and 6% had good knowledge regarding phlebitis. **Conclusions:** This study concluded that bedside staff nurses have insufficient knowledge regarding phlebitis. This poor knowledge can reduce the effectiveness of nursing care provided to the patient. Therefore, educational sessions and interventional study needed to enhance their knowledge regarding phlebitis.

INTRODUCTION

Health promotion, better results, and the restoration of health and well-being all benefit from nursing care in hospitals. Peripheral intravenous cannula maintenance, monitoring, and care are all included in this [1]. Administration of parenteral medicine is an essential component of intravenous therapy and an integral part of the nursing field. Nursing staff monitor, administer and provide care to the patients prescribed by the clinicians or doctors [2]. Phlebitis is a common, avoidable complication faced by patients during intravenous therapy. In the modern era, Intravenous therapy is an essential and main component in medicine and treatment [3]. Intravenous therapy meets the patient's needs for fluid, nutrients, medicines and blood products [4]. Phlebitis is the inflammation of the vein inner layer of venous tunica intima called phlebitis [5]. The complications that commonly occur due to phlebitis are erythema, pain, swelling, and palpable thrombosis of the cannulated vein [6]. Furthermore, between 2017 and 2021, there were 1.82 instances of phlebitis for every 100 days when a venous catheter was used [7]. A recent study showed that 80 participants (6.1%) out of 1,319 experienced phlebitis.

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Reduced mobility (p = 0.015), family history of deep vein thrombosis (p = 0.05), catheterization of veins on the back of the hand (p = 0.012), pain (p 0.01), Amoxicillin-Potassium Clavulanate (p = 0.015), and Omeprazole Sodium (p = 0.029) were all linked to the development of phlebitis [8]. Moreover, phlebitis may classify into four different types on the basis of basic factors [9]. These are mechanical, infectious, chemicals and post-infusion phlebitis [10]. There are some patient factors such as high age, female gender and some diseases conditions (malignancy, immunosuppression and malnutrition) that cause and increase the risk of developing phlebitis [11]. Staff nurses play an essential role in minimizing the rate of phlebitis and the complications of phlebitis in the patients who receive medical care [12]. So, this assesses the current knowledge of nurses regarding phlebitis.

METHODS

This study was performed to investigate nurses' current knowledge regarding phlebitis. This study used a cross-sectional, quantitative approach with a sample size of 100 bedside nurses. It was conducted with a convenient sampling technique from December 2022 to April 2023 at a private-sector tertiary care hospital in Karachi, Pakistan. The study population was registered nursing staff who were working in different wards in the hospital. Registered Nursing staff (RN) and graduated nursing staff (BScN) with a working experience of 6 months with voluntary participation are included in the research. Licensed practical nurses, practical nurses, nursing staff not willing to participate and nurses with less than six months of experience were excluded from the study. With a population of 150, the sample size was determined using open EPI version 3 and a 95% confidence interval. The size of the obtained sample is 100. The data were collected by a self-administered questionnaire with 15 questions and demographic characteristics. The knowledge scoring system is 0-2, where 0 means don't know, 1 means no, and 2 means yes. The total score of the tool is 30, and below 50% is considered low-level knowledge, 50% to 70% is average-level knowledge, and above 70% is considered good-level knowledge. This study data were computed and analyzed in Social Package for Statistical Science (SPSS) software version 22.0. Inform consent was taken from each participant before filling out the questionnaire. We ensured our participants from any potential psychological, physical or social harm. This research was conducted after permission from a selected private tertiary care hospital, and study approval was taken from the Institute.

RESULTS

The table presents the results of a study involving 100 Nurses. It includes variables such as gender, age, job rank, experience, healthcare setting, and level of education. Among the participants, 74% were female, and the majority fell within the age range of below 30 years (51%). The most common job rank was staff nurse (89%); nearly half of the participants had 1-5 years of experience (49%). The medical setting was the most common (64%), and most participants had the educational qualification of a registered nurse (65%). The table provides a concise overview of the demographic and professional characteristics of the study participants.

Table 1: Demographic characteristics of the participants n=100

Name of variable, Response/ Category	Frequency (%)
Gender	
Male	26 (26)
Female	74(74)
Total	100(100)
Age	
<30 Years	51(51)
30-45 Years	32(32)
45 > Years	17(17)
Total	100(100)
Nurse In charge	11(11)
Staff Nurse	89(89)
Total	100(100)
Experience	
6 months -1 year	25(20)
1-5 years	49(49)
6-10 years	26(26)
Total	100(100)
Healthcare Setting	
Medical	64(64)
Surgical	25(25)
Maternal child health sections	5(5)
Emergency outpatient department	6(6)
Total	100(100)
Level of Education	
Registered Nurse	65(65)
Bachelor	35(35)
Total	100(100)

Table 2 shows the result of the overall level of knowledge among 100 participants; 50% of participants have inadequate knowledge regarding phlebitis, 44% have average, and 6% have good knowledge regarding phlebitis.

Table 2: Levels of knowledge Regarding Phlebitis

Knowledge Level	Frequency (%)
Inadequate	50(50)
Average	44(44)
Good	6(6)

DISCUSSION

With an incidence rate of 20% in Pakistan, 27.7% in India, and 4% in the United States, phlebitis is a serious public health concern [13]. The nursing team at the patient's

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bedside is crucial in the early diagnosis and treatment of phlebitis [14, 15]. The nursing staff, however, lacks an understanding of phlebitis, which could result in subpar patient treatment and elevated patient risks. This study evaluates the level of phlebitis knowledge held by bedside nursing staff. In this regard, a study concluded that nursing interventions for preventing and managing the occurrence may be (re)designed given the prevalence of known phlebitis [10]. Present findings show that only 6% had good knowledge regarding phlebitis. Another study from India found that 13.5 had good knowledge [16]. In contrast, a study from Nepal found that 82.47% of respondents had good knowledge [17]. Additionally, more than half of the nurses were unaware that the cannula's material and diameter could influence the frequency of phlebitis [18]. These findings may be due to varying countries' or healthcare facilities' training and educational programs for nursing workers that can produce varying levels of knowledge. As a result, it is necessary to recognize the most frequent potential dangers associated with continuing to support phlebitis to minimize pressure damage prevention and management and improve the standard of healthcare services provided in hospitals [19]. Moreover, the present findings show that 50% had inadequate knowledge regarding phlebitis. In this regard, another study shows that 38.5% of nurses had poor knowledge study recommended that nurses enhance their infusion knowledge and abilities to lessen difficulties and discomfort caused by infusion [20]. Similarly, another study by Rai *et al.*, found that 19.80 was the low mean score for pretest knowledge regarding phlebitis. The study suggested that the knowledge score of nursing staff improved when the structural instruction plan was implemented. Therefore, it can be said that educational intervention was successful [21]. Moreover, another study found that most nurses lacked sufficient knowledge of phlebitis and suggested that nurses did not adhere to current recommendations and required further knowledge and ongoing education [22]. Present findings show that 44% had average knowledge regarding phlebitis. At the same time, a study from India reported moderately adequate knowledge (53.4%) [16]. Another study found that most students (60.6%) had fair knowledge [23]. The frequency of phlebitis and other problems will likely be reduced with proper insertion technique and venous catheter management. Therefore, nurses' ongoing education is crucial [7]. The study's results demonstrated that using a standardized Peripheral Venous Catheter (PVC), care package can improve the detection and assessment of phlebitis and help lower its incidence. The audit approach helped put the research into practice since it allowed for post- and pre-implementation evaluations of the nurses' compliance with the PVC care bundle [24].

CONCLUSIONS

These findings point to a significant knowledge gap among the participants, which can impact patient care and safety. Targeted educational initiatives are required to raise the knowledge and awareness of the bedside nursing staff to provide the best patient outcomes and prevent complications linked to phlebitis.

Authors Contribution

Conceptualization: MHS, RA
Methodology: TA
Formal Analysis: TA
Writing-review and editing: AM, IK, MJK, AB

All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

The authors declare no conflict of interest.

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Original Article

Risk of Macular Toxicity After Intra-Cameral 1mg/0.1 ml Cefuroxime for Endophthalmitis Prophylaxis in Phacoemulsification Cataract Surgery

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ABSTRACT

The world's leading culprit of preventable blindness is cataracts. For numerous decades, postoperative endophthalmitis has instilled terror as a potential complication of cataract surgery. **Objective:** To determine the frequency of retinal toxicity in terms of transient macular edema following using per-operative intracameral cefuroxime 1mg/0.1ml for endophthalmitis prophylaxis. **Methods:** A Descriptive case series was done at LRBT Eye Hospital, Lahore, from 15th Dec 2020 to 14th Jun 2021. A total number of 118 senile cataract patients were included. After cataract surgery, an intracameral 1 mg injection of cefuroxime was given to each patient. The optimally corrected visual acuity and macular thickness at the center of the retina on OCT were assessed postoperatively at week 1. If they were found to be elevated, it was labeled as retinal toxicity. Data were collected on data collection proforma. **Results:** The average age of the participants was 59.68 ± 5.28 years. Mean visual acuity before and after surgery was 2.01 ± 0.74 and 1.92 ± 0.94, respectively. Mean central macular thickness before and after surgery was 241.08 ± 4.73 and 248.74 ± 5.86 µm, respectively. There were 71 (60.17%) male and 47 (39.83%) female patients. There were 42 (35.59%) farmers, 40 (33.90%) job holders, 05 (4.24%) business people, and 31 (26.27%) non-working patients. Retinal toxicity was found in 54 (45.76%) patients. **Conclusions:** Intracameral injection of cefuroxime sodium can result in transient macular edema and retinal toxicity. In this study, retinal toxicity occurred in 45.8% of patients undergoing phacoemulsification.

INTRODUCTION

Cataracts are the leading cause of blindness worldwide, accounting for over 90% of blindness in wealthy economies. The prevalence of visually significant cataracts rises with age, and they are the leading cause of decreased visual acuity in the elderly, particularly nursing care residents [1]. The prevalence of age-related cataract subtypes, such as nuclear, cortical, and posterior subcapsular cataracts, varies by population [2]. Cataract surgery is a safe and cost-effective way to treat cataracts. However, postoperative endophthalmitis is still a feared complication that results in poor visual outcomes [3, 4]. The "European Society of Cataract and Refractive Surgeons (ESCRS)" suggests using intracameral cefuroxime (1 mg/0.1 ml) after cataract surgery to lower the risk of endophthalmitis, which has been found to reduce the risk of infection significantly [5]. While intracameral cefuroxime effectively avoids endophthalmitis, there are worries about its potential retinal damage, notably macular

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edema. Cases of retinal edema following intracameral cefuroxime injection have been described in studies with varied incidence rates [6]. This study looks at retinal toxicity in the form of macular edema after a prophylactic intracameral injection of cefuroxime 1mg/0.1ml at the end of phacoemulsification cataract surgery. Because retinal edema induced by toxicity usually resolves within the first postoperative week, central macular thickness (CMT) assessed using spectral domain optical coherence tomography (SD-OCT) before and at the end of the first postoperative week [7, 8]. The findings of this study provided crucial information on the frequency of retinal toxicity after intracameral cefuroxime injection. This information aid in pre-operative patient counseling, informing them of the likelihood of toxicity and potential clouded vision following surgery. By notifying patients beforehand, we aim to reduce the morbidity of hazy vision and ensure improved postoperative results [9].

METHODS

A descriptive case series was done at LRBT Eye Hospital Multan Road, Lahore, from 15th Dec 2020 to 14th Jun 2021. The sample size of 118 patients is determined using the 95% confidence level, a 9% error margin, and the assumption that the anticipated percentage of retinal toxicity will be 46 ± 6. Non-probability consecutive sampling technique was utilized. Inclusion criteria were senile cataract patients booked (according to operational definition) for phaco with clear cornea and good pupillary dilatation, age group 51-70 years, and both male and female patients. Exclusion criteria were comorbidities such as diabetes (BSR > 200mg/dl), hypertension (BP>160/90), maculopathies, retinal vascular disorders, uveitis, NS+++, and more complex, complicated cataract surgery, previous ocular surgery, or trauma**.** After taking permission from the ethical committee of LRBT hospital and informed consent, patients enlisted for phacoemulsification were evaluated preoperatively and postoperatively. The preop assessment included visual acuity and fundoscopy to check the retina for comorbid and OCT. After cataract surgery, an intracameral 1 mg injection of cefuroxime was given to each patient. To prepare 1 mg cefuroxime, 250 mg cefuroxime injectable powder was admixed with 2.5 ml of normal saline. 0.1 ml of the resulting solution was diluted again in 0.9 ml of normal saline to achieve the desired concentration of 1 mg in 0.1 ml. The postop assessment included optimally corrected visual acuity and macular thickness at the retina's center on OCT at week 1. If found to increase, it was labeled as retinal toxicity. Data were collected on data collection performance. SPSS version 20.0 for Windows was used to analyze the data. To illustrate the age of the patients, the means and standard deviations were employed. Frequency and percentage were used to present gender, occupation, and retinal toxicity. Effect modifiers such as age, gender, pre-operation visual acuity, and occupation were controlled through stratification. Chi-square analysis post-stratification was used. Statistically significant values were defined as p-values less than 0.05.

RESULTS

The participant of this study had an average age of 59.68 ± 5.28 years. The minimum and maximum ages were 51 and 70, respectively. Visual acuity score before surgery was 6/12 in 32 (27.1%) patients, 6/18 in 53 (44.9%) patients, and 6/24 in 33 (28.0%) patients (Table 1). Stratification based on gender was also performed, and there was no association of gender with retinal toxicity. In males, retinal toxicity was found in 33 patients, and in females, retinal toxicity was found in 21 patients. This difference was statistically insignificant, with a p-value of 0.848.

Table 1: Descriptive statistics of visual acuity before surgery

Visual Acuity	Frequency (%)
6/12	32(27.1)
6/18	53(44.9)
6/24	33(28)

Mean visual acuity after surgery was 6/6 in 46 (39.0%) patients, 6/9 in 47 (39.8%) patients, 6/12 in 14 (11.9%) patients, and 6/18 in 11 (9.3%) patients (Table 2).

Table 2: Descriptive statistics of visual acuity after surgery

Visual Acuity	Frequency (%)
6/6	46(39)
6/9	47(39.8)
6/12	14(11.9)
6/18	11(9.3)

The mean central macular thickness before surgery was 241.08 ± 4.73 µm. The minimum central macular thickness was 231 µm, and the maximum was 249 µm (Table 3).

Table 3: Descriptive statistics of central macular thickness before surgery

Central Macular Thickness before Surgery (µm)	
Mean ± SD	241.08 ± 4.73
Minimum	231
Maximum	249

The mean central macular thickness after surgery was 248.74 ± 5.86 µm. The minimum central macular thickness was 239 µm, and the maximum was 260 µm (Table 4).

Table 4: Descriptive statistics of central macular thickness after surgery

Central Macular Thickness after Surgery(µm)	
Mean ± SD	248.74 ± 5.86
Minimum	239
Maximum	260

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Retinal toxicity was found in 54 (45.76%) and not in 64 (54.24%) patients (Figure 1).

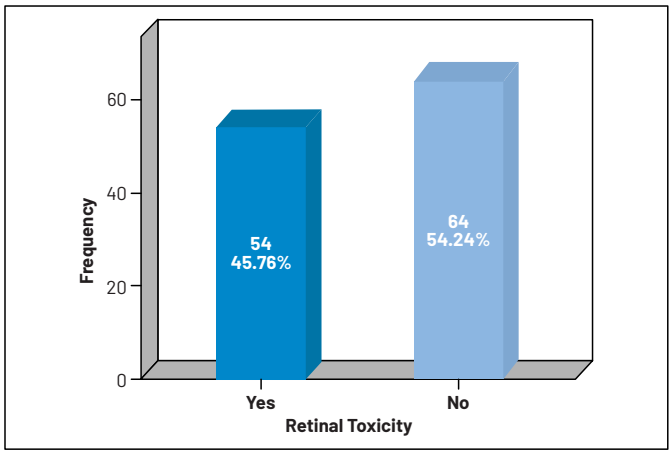

Figure 1: Frequency of retinal toxicity

Stratification was also done based on visual acuity score; in patients having pre-operative visual acuity of 6/12 to 6/18, retinal toxicity occurred in 34 patients and 20 patients having visual acuity of 6/24 (Table 5).

Table 5: Stratification of visual acuity before operation to determine the association of visual acuity before operation with retinal toxicity

Visual Acuity Before Operation	Retinal Toxicity		p-value
	Yes	No	
6/12 to 6/18	34	51	0.07
6/24	20	13	

There were more males as compared to females. There were 71 (60.17%) male and 47 (39.83%) female patients. On the frequency of occupation, there were 42 (35.59%) farmers, 40 (33.90%) job holders, 05 (4.24%) business people, and 31 (26.27%) not working patients. Age Stratification was performed, and age was not associated with retinal toxicity. In patients aged 51-59 years, retinal toxicity was found in 23; in patients aged 60-70, it was found in 31. This difference was statistically insignificant, with a p-value of 0.190 (Table 6).

Table 6: Stratification of occupation to determine the association of occupation with retinal toxicity

Occupation	Retinal Toxicity		p-value
	Yes	No	
Farmer	21	21	0.163
Job Holder	17	23	
Businessman	0	05	
Not working	16	15	

DISCUSSION

Our study investigated retinal toxicity following cataract surgery with intracameral cefuroxime. This contrasts with studies on endophthalmitis prevention and risk factors conducted by Ciulla *et al.*, Montan *et al.*, and the Endophthalmitis Study Group [10-13]. While earlier research has demonstrated the usefulness and safety of intracameral cefuroxime in preventing endophthalmitis, our investigation focused on a significant possible side impact linked with cefuroxime use. This is especially significant given the widespread usage of cefuroxime as a prophylactic measure to avoid endophthalmitis, as Faure *et al.*, and Czajka *et al.*, have highlighted [14, 15]. We discovered a high rate of retinal toxicity (45.8%) in patients receiving intracameral cefuroxime after cataract surgery. This finding is similar to prior studies by Cardascia *et al.*, and Brouzas *et al.*, who also discovered retinal edema following cefuroxime injection. However, it is crucial to note that, as mentioned in our study, some previous studies reported lower occurrences of macular edema [16-18]. It is important to mention that cefuroxime has been utilized to prevent cataract surgery [19, 20]. For many years it has been used to assist in reducing the occurrence of endophthalmitis, as Besozzi *et al.*, and Lam *et al.*, have highlighted. However, our research underlines the potential retinal damage associated with its use, emphasizing the importance of further research [21-24].

CONCLUSIONS

Our findings demonstrate that intracameral administration of cefuroxime sodium can result in temporary macular edema and retinal toxicity. In this study, retinal toxicity occurred in 45.8% of patients undergoing phacoemulsification.

Authors Contribution

Conceptualization: MHJ, SZ
Methodology: AK, AS
Formal Analysis: MBA
Writing-review and editing: MHJ, SZ, AK, AA, MBA, FS

All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

The authors declare no conflict of interest.

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Original Article

College Students' Struggles with Career Decisions and Their Personality

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ABSTRACT

Students face challenges while selecting a career in Pakistan is very common. 99% students lack career counselling services in schools, colleges and universities. In the current study career decision-making difficulties faced by students in Peshawar was investigated when they plan to apply in a school, college and university and to evaluate what kind of assistance they need in their career choices related to their personality. **Objective:** To see how personality affect the decision-making of careers in students at high schools, colleges, and universities. **Methods:** The influence of personality traits (Extraversion and Neuroticism) on the decision-making of career difficulties was investigated using a causal-comparative study methodology. In Pakistan, 99 percent of pupils still need career guidance. As a result, three hundred and seventy-six (N=376) students were chosen from Peshawar's various schools, colleges, and universities. Two questionnaires were used to gauge the participants' responses: The career decision-making difficulties Questionnaire and Big Five Personality Inventory. **Results:** Findings suggest that most students needed help with professional decision-making and that a small percentage of students were satisfied with their selected disciplines. **Conclusions:** Students with high neuroticism and low extroversion had difficulty making professional decisions.

INTRODUCTION

Historically, choosing a Career or profession has been seen as less stressful and more straightforward some years ago. In general, a person's career is decided mainly by following their father's footprints, so a child of a carpenter would also become a carpenter in the future, and a child of a cobbler would also learn how to become a cobbler like his father; however, the most honorable and well-off high-class people prepare their children to be upcoming pioneers. This process of young people choosing their career has changed dramatically, mainly since the industrial revolution has grown increasingly complicated and perplexing. In the twenty-first century, the numerous professional paths and many employment opportunities make this decision-making process even more challenging [1]. Further widespread entrance of students into higher education, the large number of females arriving in the workforce, and the swing from industrial development to service-based enterprise in several developed economies have influenced how people choose their careers. In contrast, the old-style outlook of deciding on a career only once in a lifetime has become obsolete and has been replaced with the notion that choosing a career is a lifelong process [2]. Today's new generation make multiple consecutive decisions, evaluate their former professional choices, and change their behaviors and ambitions regularly. Job counseling is critical in assisting people in being much more aware of their options and making informed decisions about many disciplines and available

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career opportunities that best suit their personalities. An academic atmosphere is designed to encourage and support a job choice well-suited to one's personality type. There are a variety of elements that influence one's decision to pursue a particular career path. Borchert identified personality, opportunities and environment as important factors for career decision-making. However, the most critical aspect in determining one's professional path is the individual's personality and desire to pursue a specific career path [3]. Feldman proposed that personality characteristics, professional interests, demographic position, early job experiences, familial contexts, and implications are part of professional decision challenges [4]. Personality is the unique, relatively long-lasting internal and external characteristics of a person's character that impact conduct in various settings [5]. In the big five personality models, five traits have been classified as 'wide' since they have been shown to unite numerous perspectives and domains. [6]. Neuroticism, agreeableness, openness to experience, extraversion, and conscientiousness are measurable components of personality. Investigators consistently perceive and agree about personality traits and their relevance in the professional decision-making procedure (Figure 1) [7]. Agreeing with the model of Gati, which categorizes personality characteristics, individuals with more emotional stability are predicted to face fewer issues in professional decision-making both beforehand and during the career decision-making process [8]. Studies have found adverse associations between occupational decision-making challenges [9] and extraversion and emotional stability characteristics, supporting the significance of personality traits [10]. It was found that personality relates to complications of professional decision-making independent of educational environment and age when the influence of personality on career indecision was explored with the questionnaire on Career Decision-Making Difficulties. Another study found perfectionism, more agreeableness, neuroticism, and the need for psychological inference considerably linked with emotional and personality-related professional challenges [11]. Personality qualities have been linked to challenges in making job decisions. [12].

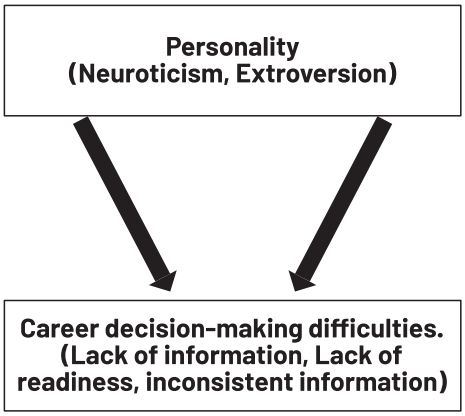

Figure 1: Conceptual model of the study

In Pakistan, students must go through three stages of professional decisions. Students must choose a career during Matriculation, Intermediate, and Bachelor studies. After completing eighth grade, students must choose a career route that will allow them to pursue future opportunities. They can pick either Science or Arts. Each group has various mandatory and core subjects. After matriculation, students are enrolled in colleges and typically have merely two months to select a career. Subject choices in secondary education often reflect their career path. So, it is highly encouraged to get guidance now. This allows them to carefully weigh the options of General Science, Commerce, Computer Science, Fine Art, Pre-Engineering, and Pre-Medical. Then, at the bachelor's level, career counselor assesses the student's financial situation and academic performance, recommending disciplines such as medicine, business, arts & humanities, management, engineering etc. At every step, students choose subjects that lead to a relevant career. Choosing a career is a challenging task that requires careful thinking and concentration. Many people can make such choices easily, but many others have difficulty. These concerns and issues cause hazards in decision-making, preventing accurate choices [13]. Due to a lack of competent career guidance, these issues are prevalent in Pakistan. To compensate for the lack of career counseling and decision-making skills, students rely on their friends and family members for career advice, which causes them confusion and makes them dependent on their friends and elders for career advice, which causes them to lose their ability to think for themselves. This causes students to choose the wrong professional path, and instead of being inspired by their jobs or majors, they are demotivated and lose their passion for movement. Adolescence is still in the fog of a new round of choices, which causes pupils to pick an inappropriate professional route, further demotivating them. Their inability to focus and be excited about their subject prevents them from giving their best. Counselors can help students make career choices by learning about

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their challenges and helping them overcome or at least reduce them. The current study sought to depict and characterize the numerous career-related decision-making challenges, Pakistani students face. Understanding the underlying causes of issues is critical since it might determine the severity and the type of response necessary. The study sought to discover the effect of personality on challenges of professional decision-making among Peshawar students. The study also compared male and female students' professional decision-making challenges. This study also includes to analyze the influence of Neuroticism and Extroversion in students' career decision-making difficulties.

METHODS

In this research, a causal-comparative research design was used that was questionnaire-based survey. From the heads of institutions, permission was taken and information was collected from different schools, colleges, and universities in Peshawar. The sample comprises three hundred and seventy-six participants (N=376), selected through a stratified purposeful sampling technique (Figure 2). Three strata were made based on educational level. The first strata consisted of school-level students in which only students of grade 8th, 9th, and 10th were selected. The second stratum consists of college-level students and third stratum consists of university-level undergraduate (BS and Masters) students. Each stratum consists of same number of students and equal number of male and female students.

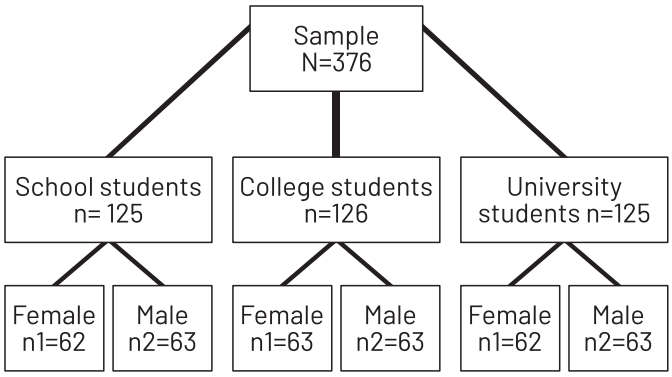

Figure 2: Flowchart of students selected for the study

The sheet of demographic information was used to obtain basic info about the participants. Then two scales, Career Decision Difficulties Questionnaire (CDDQ) and Big Five Personality Inventory (BFI) subscales (Neuroticism and Extraversion) were administered. Before filling the questionnaires instructions were given to the participant. They were guaranteed the confidentiality of the data. Participants were also requested to carefully read and then fill questionnaires. In the end, the respondents were appreciated for their cooperation and involvement in the study. After data collection, all the analyses were done with the help of SPSS version-21.0.

RESULTS

Table 1 showed number of items and Cronbach's alpha reliability of Career decision-making difficulties questionnaire (CDDQ) and Big Five Personality Inventory. It indicated that these scales were reliable.

Table 1: Psychometric properties of scales (N=376)

Measure	No of items	Alpha coefficient
Big Five Personality Inventory	44	.78
Career Decision Difficulties Questionnaire	34	.89

Table 2 showed the frequencies and percentages of the educational level of the participants. The frequency of both Matric and University level students was 125, while the frequency for college-level students was 126. The table also indicated that 33.2% of matric level, 33.6% of intermediate level, and 33.2% of university level students participated in the research.

Table 2: Frequency table of Educational Level of Participants (N=376)

Educational Level	F (%)
Matric	125 (33.2)
FA/FSC	126 (33.6)
BS/B.SC/Master	125 (33.2)
Total	376 (100)

Table 3 showed One Way Analysis of Variance (ANOVA) of the scale of career decision-making difficulties among students of all three groups (school, college, and university). The mean score of a school with standard deviation was 154 ± 43.03, and the mean score of a college with standard deviation was 156.6 ± 45.4, while the mean score of the university with standard deviation was 156.6 ± 45.8. The result showed no significant variance between school, college, and university students

Table 3: ANOVA (One way) and means standard deviations on career decision-making difficulties questionnaire of school, college, and university students (N=376)

	School	College	University		
Scale	M ± SD	M ± SD	M ± S.D	F(1,294)	η^2
CDDQ	154 ± 43.03	156.2 ± 45.4	156.6 ± 45.8	.075	.928

Table 4 indicated that the mean score of career decision-making difficulties scale with standard variation was 155.5 ± 42.8 and the mean score of subscale neuroticism with standard variation was 24.1 ± 5.06 while the subscale Extraversion mean score with standard variation was 25.4 ± 5.46 among all three levels (School, College, and University). Results indicated a positive relationship between the neuroticism subscale and career decision-making difficulties scale (r=.040) which showed that neurotic students would face more difficulties in their careers. Results also indicated a significant negative correlation between the Career decision-making

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difficulties scale and Extraversion, which was (r= -.127 **). This means that extroverts will face fewer career decision-making difficulties.

Table 4: Descriptive Statistics and correlation for Career Decision-Making Difficulties scale with subscale Neuroticism and subscale Extraversion (N=376)

Variables	n	M ± SD	1	2	3
Career Decision-making Difficulties	376	155.5 ± 42.8	-	-	-
Neuroticism	376	24.1 ± 5.06	.020	-	-
Extraversion	376	25.4 ± 5.4	-.127*	.400**	-

DISCUSSION

The main objective of this research was to determine the effect of personality on career decision-making issues among students. The impact of neuroticism and extraversion on challenges of career decision-making was investigated. Furthermore, obstacles in selecting career decisions were compared among high school, college and university students. It was discovered that all three levels of students (school, college, and university) in Pakistan have difficulty selecting career decisions. Various studies show that personality strongly impacts career decision-making problems. Both the scales Career decision difficulties questionnaire (CDDQ) = .89, and Big five personality Inventory =.78) were reliable and internally consistent for the current sample, according to reliability analyses. According to the study findings, there is no substantial variance between all these three levels. (School, college, and university). Furthermore, these findings also demonstrate that students at all these three levels struggle to make career choices. The findings also show that in Pakistan, students, even at the level of master's, are perplexed about their job options, and they are confronted with obstacles and continue to struggle with career decisions. These findings are also confirmed by the fact that 99 percent of Pakistani students do not have access to career counseling and most students choose a vocation based on a family's agreement, devotion to a companion, or preoccupation with an ideal. Almost no occupation is chosen logically based on aptitude tests or other psychological measures. The results reveal that neuroticism and career decision-making difficulties have a substantial positive relationship. These findings are in line with prior studies. Students who scored high on career hesitation or were unsure about their career choice also had high levels of neuroticism [14, 15]. Neuroticism seems to be related to underperformance because the emotional constituents in the career decision-making process are involved. It was found that neuroticism is associated favorably with dependent decision-making and adversely connected with problem-solving impairments [16]. To minimize their perceived stress level, neurotic people appear to be watchful more in their job hunt as well as impulsive in the decision-making of their career [17]. The study's findings also show a negative correlation between Career decision-making difficulties and Extraversion. These findings align with earlier research, which found that high extroversion is associated with fewer difficulties in making career selections [18]. Extraversion is essential in job development, helping the quest for information about potential careers [19]. According to Van Hooft *et al.*, extrovert individuals seek social support and are more persistent in their quest when they are having difficulty finding work [20].

CONCLUSIONS

The main goal of the current research was to determine the impact of personality on career decision-making challenges in students. Results demonstrate that student's at high school, college, and university encounter significant challenges in making career options. As a result, there is a requirement for career counseling facilities in Peshawar for all students at all stages of school, college, and university to overcome or, at minimum, mitigate these challenges. The research findings also demonstrate that personality has a considerable impact. A high level of neuroticism has a negative impact on job decisions, whereas a high level of extraversion has a beneficial impact. The current study was conducted with limited resources, a small sample size, and a short time frame. Data were gathered by self-report questionnaires, which are susceptible to participant bias. Students from various educational levels (Matric, Intermediate, and University) were included in the study, which tainted the results and complicated the analysis. For each component, data were collected using only one specific metric (personality and career decision-making difficulties). However valid and reliable these psychometric tools may be, they cannot comprehensively and thoroughly assess these constructs.

Authors Contribution

Conceptualization: HA
Methodology: SA, HA
Formal analysis: HM, SA
Writing-review and editing: HA, SA, HM

All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

The authors declare no conflict of interest.

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Original Article

Correlation of Risk Factors with the Severity of Diabetic Retinopathy at a Rural Health Facility in Sindh Pakistan

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ABSTRACT

Diabetes Mellitus (DM) and the resulting Diabetic Retinopathy (DR) is a significant health problem around the World. In 2019, the total number of diabetics worldwide was 463 million, and 35% had some DR. **Objectives:** To determine the correlation between the severity of Diabetic Retinopathy (DR) and the known risk factors. **Methods:** Analytical cross-sectional study design was used with convenience sampling in a primary, multispecialty day care health facility under the Baqai Foundation (Khushal Nagar) in a rural area of Sindh from 2020 - 2022. A total of 133 patients had some DR according to the International Classification of Diabetic Retinopathy Severity Scale (ICDRSS), which correlated with the different risk factors. Spearman rank correlation was used, and the result was considered significant when the P value was <.05. **Results:** The results showed a significant positive correlation between the severity of DR with Age, Random Blood Sugar, Hypertension, and Smoking. Glycated hemoglobin and hyperlipidemia were not significantly correlated, mainly because of the small sample size. (23 and 14 respectively). The patients who tried to have Lipid Profile and Glycated Hemoglobin done had stage four or five of ICDRSS. **Conclusions:** Most risk factors studied were positively correlated with the severity of DR. Besides the intended study, the findings highlighted the non-awareness of patients about DR and its consequences. Awareness campaigns and screening programs for DR and its risk factors are urgently required and tailored to our circumstances.

INTRODUCTION

Diabetes Mellitus (DM) and the resulting Diabetic Retinopathy (DR) is a significant health problem around the World. In 2019, the total number of diabetics worldwide was 463 million, and 35% had some DR [1]. Pathogenesis of DR remains unclear, although various factors are known to be operative, such as a high glucose environment [2], accumulation of leukocytes [3], and Aldosterone [4]. These can all lead to loss of pericytes, increased permeability of retinal blood vessels, and ischemia-induced vascular proliferative changes, leading to macular edema and proliferative retinopathy. Although the true prevalence of DR among diabetic patients in Pakistan is unclear [5], it has variously been reported as 11.77% [6], 24.2% [7], 28.78% [5], 55.3% [8], and 56.9% [9]. The treatment of DR has become much more effective in the last few decades. However, it is still the leading cause of blindness worldwide [10], although the burden of diabetic blindness is shifting from rich to poorer countries [11]. Prevention or delaying the development of DR remains the ideal management, and the reduction of controllable risk factors is crucial to accomplish this. Several risk factors promoting the development of DR have been identified,

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such as hyperglycemia [12], Increasing age, duration of DM, hypertension, hyperlipidemia, and family history of DM [13]. The frequency of risk factors among the Pakistani rural population has not been extensively reported [7]. Hence, even modest information in this regard may help further research. Therefore, this study has been conducted to determine the correlation between risk factors of DR and the severity of DR in Gharo, district Thata, Sindh.

METHODS

Analytical cross-sectional study design was used with a non-probability, convenient sampling technique. The study was conducted in a primary, multispecialty daycare health facility under the Baqai Foundation (Khushal Nagar) in a rural area near Gharo, Thata District of Sindh. The selection criteria of the patients were those patients who attended the Eye OPD from 1st April,2020 to 30th June,2022 at Khushal Nagar, a primary, multispecialty daycare health facility under the Baqai Foundation in a rural area near the town of Gharo, district Thata. The patients referred from other departments for evaluation of DR, and the non-referred Eye OPD patients whose loss of vision was not explained fully by any anterior segment findings, underwent ophthalmoscopy at the slit lamp with a 90 D lens. If we discovered DR, we graded it according to the International Clinical Diabetic Retinopathy Severity Scale (ICDRSS) [14]. In patients with DR, the history included determination of age, sex, smoking, and any other medical conditions known to the patient. The blood pressure (BP) and the random blood glucose (RBS) levels were determined at the Clinic. At the same time, for lipid profile and glycated hemoglobin (HbA1C), the patients were asked to get it done, at a subsidized cost, from the laboratory of the Tertiary Center (Baqai Medical University). We excluded from the study any patient whose opaque media did not allow proper DR classification or was missing from the record for any reason. After the exclusion according to the set criteria, some degree of DR was found in 133 Patients (male and female included) with ages ranging from 32 to 78 years. The correlation of different risk factors was determined among these DR patients. Hence Stage 1 of the ICDRSS was not considered. The relevant institutional review board (IRB) obtained ethical approval for the study. This approval ensures that while conducting the study, ethical principles and protection of the rights and well-being of the participants are considered. The study ensured ethical considerations by obtaining a signed consent from the willing participants and assuring the confidentiality of their information. After data compilation, SPSS version 20.0 was used for the data analysis. Frequency and percentage were used for the demographic variables. Moreover, Spearman rank correlation was used to determine the correlation between DR severity and different risk factors, and the result was considered significant when the P value was <.05. Each risk factor was correlated separately and independently.

RESULTS

Table 1 shows that there are a total of 133 patients. Of these, 94 patients (70.7%) are male, and 39 (29.3%) are female. Regarding their ages in the 32-42 age groups, there were 4.5% participants. Moreover, the 43-52 age group comprises 9.3%. 53-62 age group, which is 60%. In the 63-72 age group, 21.2% of the participants are. Last, the 73+ age group there is 5% of the participants.

Table 1: Sociodemographic characteristics n=133

Gender	Number of Patients (%)
Male	94 (70.7%)
Female	39 (29.3%)
Age	
32-42	6 (4.5%)
43-52	12 (9.3%)
53-62	80 (60%)
63-72	28 (21.2%)
73+	7 (5%)

Table 2 displays, the sverity of DR among participants of stage I, II, III, IV and V which is 0 (0%), 60 (45.11%), 40 (30.07%), 25(18.8%)and 8(6.01%) respectively.

Table 2: Severity of DR through International Classification of Diabetic Retinopathy Severity Scale

Stage	Dilated pupil ophthalmoscopy findings	Severity	N=133
I	No diabetic Retinopathy (DR)	No DR	0 (0%)
II	Only Micro-aneurysms	Mild None Proliferative NPDR	60 (45.11%)
III	Presence of - micro-aneurysms, - intra-retinal hemorrhages - and/or venous beading BUT NO FEATURES OF SEVERE NPDR	Moderate NPDR	40 (30.07%)
IV	4-2-1 Rule (Any or more of the following) - hemorrhages in all four quadrants -2 quadrants or more have venous beading -1 quadrant or more of Intra retinal Micro -angiopathy. (IRMA)	Severe NPDR	25 (18.8%)
V	- Neo-vascularization of the disc (NVD), or elsewhere (NVE) - Vitreous hemorrhage - Pre-retinal hemorrhage	Proliferative diabetic retinopathy" (PDR)	8 (6.01%)

Table 3 shows correlation between the severity of Diabetic Retinopathy with Age, Random Blood Sugar, Hypertension, and Smoking. Glycated hemoglobin and hyperlipidemia were not significantly correlated, mainly because of the small sample size. (23,14). The patients who tried to have Lipid Profile and Glycated Hemoglobin had stage four or five of ICDRSS.

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Table 3: Correlation and Diabetic Retinopathy and Risk factors

Risk Factors	Spearman Correlation	p-value
Age	0.7	0.00001**
Random blood sugar	0.6	0.00001**
Blood pressure (systolic)	0.5	0.02099**
Blood lipids	0.2	0.29736
Glycated Hemoglobin (HbA1C)	0.4	0.05860
Smoking	0.5	0.00040**

**Significant

DISCUSSION

The main assessment of this study, although a simple correlation, is to bring into record whatever data was available from a health center in rural Sindh. In this study, males were 70.7% and females 23.3%; this may be due to males being more in number than females attending the OPD. Furthermore, the majority (60%) of the patients were 53-62. Similarly, a study conducted showed 57% male and 43% female, with the majority (25.4%) age group (50-54%) [8]. This study indicated a correlation of DR with age, random blood sugar, blood lipids, and smoking. On the other side, the association of risk factors with DR is consistent with other studies [12, 13, 15, 16]. Furthermore, a systematic review study stated that risk factors such as dyslipidemia and hyperglycemia are the main target of all clinicians to be controlled to prevent DR [2]. The current study showed a correlation of DR with smoking. Some other studies' results revealed that DR and smoking were positively correlated, while it is often reported otherwise [17-20]. The study's chief limitation was a lack of data about the patient's medical history, investigations, and follow-up. Hence, considering the scanty data available for this study, a simple cross-sectional correlation study design was chosen instead of a more elaborate study. Despite being educated and warned, this oblivion and neglecting attitude of the patients seems mainly due to non-awareness about the consequences of neglecting DR in the early stages. It was an un-intended observation that the only patients who traveled for lipid profile belonged to stages 4 & 5 of ICDRSS, indicating that willingness to make some effort was increased once patients lost sight significantly. This highlights the problem of non-awareness in patients about their health problems, which has often been discussed [21-24]. However, financial and domestic factors and time for travel must also have been operative. The role of risk factors in the prognosis of DR is established [25]. However, to reduce the blindness burden, timely intervention is mandatory. To achieve this, awareness campaigns [26] and screening can make the task easier. Furthermore, the screening strategies employed by financially advanced countries may not be feasible for low-income countries [27]. Strategies for screening for DR have to be tailored according to our geo-political needs and resources, as some other regional countries are planning [27].

CONCLUSIONS

Most risk factors studied were positively correlated with the severity of DR. Besides the intended study, the findings highlighted the non-awareness of patients about DR and its consequences. Awareness campaigns and screening programs for DR and its risk factors are urgently required, and tailored to our circumstances.

Authors Contribution

Conceptualization: AK
Methodology: MQK, MA
Formal Analysis: AK, MA
Writing-review and editing: AHR, MSF, AN, RAK, ABB

All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

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Systematic Review

Efficacy and Safety Profile of Lenalidomide vs Lenalidomide + R-CHOP in patients with Diffuse Large B Cell Lymphoma: A Systematic Review

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ABSTRACT

The most frequent cause of non-Hodgkin lymphoma, which accounts for around one-third of cases, is diffuse large B cell lymphoma (DLBCL). Immune chemotherapy combined with rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP) is the standard therapy for DLBCL. **Objective:** To analysing the utilization of Lenalidomide versus Lenalidomide R-CHOP regimen in treatment of DLBCL in terms of treatment efficacy and safety. **Methods:** PRISMA guidelines were followed for conducting this study. A thorough literature search was done from November 15 to November 25, 2022. A variety of databases, including PubMed, Google Scholar, and other, were used to conduct the literature search. Finally, for this systematic review, 10 studies were chosen. **Results:** In our study the monotherapy with Lenalidomide was found less significant in terms of improvement in Overall response rate, complete response among patients with DLBCL. However; Lenalidomide + R-CHOP was more effective in improving overall response rate (ORR) with ORR of 92.89% vs 30.58% and complete response rate (CRR) of 80.20% vs 12.53%. The partial response rate (PR) was comparable between two therapies. similarly, the Progression free survival was also better in combination therapy. Haematological and Non-Hematological adverse effects of grade >3 were found higher among patients with combination therapy and Neutropenia was commonly observed adverse effect. **Conclusions:** Combination therapy was associated with significant improvement in disease outcome, however; the adverse effects were reported high in combination therapy vs monotherapy.

INTRODUCTION

Non-Hodgkin lymphomas (NHL) are classified into numerous subtypes, with the aggressive diffuse large B-cell lymphoma (DLCBL) being the most frequent [1]. DLCBL is characterized by its diffuse organization, mature B-cell phenotype, and cell shape, as well as its various subtypes and genetic profiles. There are two types of germinal centres, according to the Hans classification: germinal centre type (GCB) and non-germinal centre type (NGCT) (non-GCB, encompasses most of the activated B-cell type, known as ABC-type) [2]. The conventional treatment for DLBCL is immunotherapy with rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP). It cures 50-60% of patients, although patients with relapsed/refractory (R/R) DLBCL have a poor result [3]. Despite significant progress in understanding the genetic and molecular profile of DLBCL over the last few years, there has been limited success in transferring this information into effective upfront therapies. Recently the inclusion of various medications to improve outcomes has drawn significant attention.

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Lenalidomide, a derivative of thalidomide, is an immunomodulatory agent that shows fewer side effects such as myelosuppression. In preclinical studies, Lenalidomide was found to have antineoplastic properties that boost cytotoxicity mediated by T and NK cells, as well as immunologic properties that inhibit tumour cell growth and angiogenesis in addition to directly killing cancer cells [4-6]. It not only acts through several routes, but it has also been proven to work on a wide range of hematologic malignancies, including but not limited to multiple myelomas and B-cell NHL [7, 8]. Lenalidomide is a well-tolerated medicine that, when paired with R-CHOP against DLBCL, makes it a potential therapy choice for such individuals [9]. According to long-term follow-up combined results from two phase II studies, the combination of Lenalidomide and R-CHOP maintained its efficacy over time, with a significant improvement of progression-free survival (PFS) and overall survival (OS); and very less side effects in long run. When paired with R-CHOP, Lenalidomide was shown to reduce the unfavourable prognostic effect of the non-GCB phenotype [10]. The goal of this trial, however, was to compare the safety and effectiveness of treating DLBCL with Lenalidomide vs Lenalidomide with R-CHOP.

METHODS

This study was conducted in line with PRISMA guidelines [11]. A comprehensive literature search was carried out from 15th November 2022 to 25th November 2022. The literature search was conducted through various databases like PubMed, Google scholar, EMBASE, web of science and finally Cochrane database Library. The literature search was done through various MeSH terms of paramount significance given as: "Lenalidomide" OR "Lenalidomide based regimens" OR "R-CHOP" OR "Lenalidomide + R-CHOP" OR "Diffuse large B-cell Lymphoma(DLBCL)". The clinical trial was also included for validation of this systematic review and search of various trials was done using ClinicalTrials.gov website. The PICO definition of the study is represented in tabulated form given in Table 1. The study selection was done by two potential authors (A.R and M.S.H). The studies selection was done through assessment of relevant titles, abstracts and retrieved references and those not falling under inclusion criteria were excluded. The full text articles retrieved after selection process were than assessed by two independent authors and any dispute among them was solved with the help of third author(S.M).

Table 1: Showing the PICO definition of the study

Population	Patients with diagnosed DLBCL
Intervention	Lenalidomide based monotherapy
Comparator	Lenalidomide + R-CHOP based combination therapy
Outcomes	Overall response rate, Complete response, Partial response and Progression free survival.

The standard variables of interest like author name, year of study, country of study, mean age of the patients, and study type were extracted in first place than disease specific variables of interest like disease characteristics, type of regimen given, follow-up duration, complete response (CR), partial response (PR), overall response rate (ORR), progression free survival (PFS) and finally adverse events either Haematological or Non-Haematological and >grade 3 events were extracted. The randomised controlled trials quality assessment was done through Jadad scale (11). The risk of bias was clearly identified and studies with best methodologies were opted for analysis. Data analysis were done through SPSS. V. 25, because all variables were just expressed in the form of frequency and %ages due to qualitative nature of the variables and similarly quantitative variables were expressed as mean and standard deviation, so no correlation statistics were performed.

RESULTS

The initial search retrieved about 300 articles of interest. After removing duplicates and irrelevant studies (100), 20 single arm studies depicting the usefulness of Lenalidomide and Lenalidomide + R-CHOP in DLBCL were assessed for eligibility and only 10 studies were included to synthesize our systematic review. The PRISMA flow chart for selection of final 10 studies given shown in Figure 1.

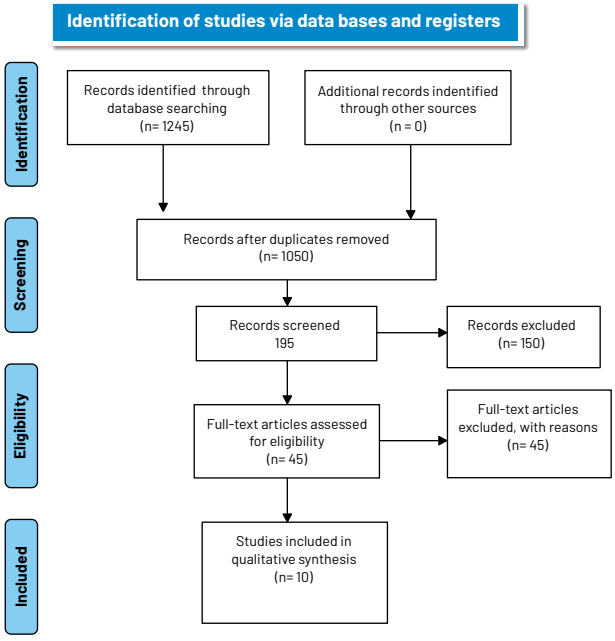

Figure 1: PRISMA flow chart of the selected studies included in systematic review

a): Efficacy profile of Lenalidomide and Lenalidomide + R-CHOP study groups:

A total of 327 patients were included in Lenalidomide study group and the mean age of the patients in Lenalidomide study group was 68.6±17.3 years. Patients with DLBCL were

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included and only randomized controlled trials were included as shown in (Table 2).

Table 2: Showing the demographic profile of the studies included in Lenalidomide study group

Authors/year of study	Country of study	Study design	Study population	Patient numbers (N)	Patient age
Mondello *et al.*, (2016) [12]	Italy	Retrospective cohort	R/R DLBCL	123	64
Witzig *et al.*, (2011) [13].	USA	Randomized control trial phase II	DLBCL	108	66
Wiernik *et al.*, (2008) [14].	USA	Randomized control trial phase II	R/R DLBCL	26	65
Czuczman *et al.*, (2017) [15].	Multi-centre	RCT Phase II/III	R/R DLBCL	51	69
Beylot-Barry *et al.*, (2019) [16].	France	RCT Phase II	R/R DLBCL leg type	19	79

According to Lenalidomide group statistics, overall response rate (ORR) was 30.58%, complete response rate (CRR) was 12.53% and partial response rate (PRR) was 17.73%. The average progression free survival in Lenalidomide group was 9.8 months with 23.5 months of follow-up. The disease specific variables of Lenalidomide group are given in (Table 3).

Table 3: Showing the effectiveness of Lenalidomide in DLBCL in terms of ORR, CR, PR, and PFS

Authors/year of study	Regimen	Dose	ORR	CR	PR	OS	PFS	Follow-Up time
Mondello *et al.*, (2016) [12]	Lenali-domide	15mg or 25 mg for 21days	46 (37 %)	21 (17 %)	24 (20 %)	73 months (7-127)	34 months (2-108)	54 months
Witzig *et al.*, (2011) [13].	Lenali-domide	25mg for 21 days	30 (28 %)	8 (7 %)	22 (20 %)	NA	2.7 months	9.2 months
Wiernik *et al.*, (2008) [14].	Lenali-domide	25mg for 21 days	5 (19 %)	3 (12 %)	2 (8 %)	NA	4 months (0-14.5)	3.7 months
Czuczman *et al.*, (2017) [15].	Lenali-domide	10mg or 25 mg for 21days	14 (27.5 %)	5 (9.8 %)	9 (17.6 %)	7.75 months	3.4 months	1.84 months
Beylot-Barry *et al.*, (2019) [16].	Lenali-domide	25mg for 21 days	5 (26.3 %)	4 (21 %)	1 (5.3 %)	19.4 months	4.9 months	49 months

A total of 197 patients were included in Lenalidomide + R-CHOP study group and the mean age of the patients in Lenalidomide study group was 66 ± 12.2 years. Patients with diffuse large B-cell lymphoma were included and only randomized controlled trials were included as shown in (Table 4).

Table 4: Showing the demographic characteristics of the studies included in Lenalidomide + R-CHOP study group

Authors/year of study	Country of study	Study design	Study population	Patient numbers (N)	Patient age
Sanjal *et al.*, (2021) [17].	USA	Randomized controlled trial Phase II	DLBCL	39	63
Nowakowski *et al.*, (2015) [18].	USA	Randomized controlled trial Phase II	DLBCL	64	65
Nowakowski *et al.*, (2011) [19].	USA	Randomized controlled trial Phase I	DLBCL	24	65
Vitolo *et al.*, (2014) [20].	Italy	Randomized controlled trial Phase II	DLBCL	49	69
Chiappella *et al.*, (2013) [21].	Italy	Randomized controlled trial Phase I	DLBCL	21	68

According to Lenalidomide + R-CHOP group statistics, overall response rate (ORR) was 92.89%, complete response rate (CRR) was 80.20% and partial response rate (PRR) was 12.69%. The average progression free survival in Lenalidomide + R-CHOP group was 23.6 months with 26.9 months of follow-up. The disease specific variables of Lenalidomide + R-CHOP group are given in (Table 5).

Table 5: Showing the effectiveness of Lenalidomide + R-CHOP in DLBCL in terms of ORR, CR, PR, and PFS

Authors/year of study	Regimen	Dose	ORR	CR	PR	OS	PFS	Follow-Up time
Sanjal *et al.*, (2021) [17].	Lenalidomide + R-CHOP	Lenalidomide: 25mg, Rituximab: 375mg/m^2, Cyclophosphamide: 750mg/m^2, Vincristine: 1.4mg/m^2, prednisone: 100mg	32 (97%)	29 (88%)	3 (9.0%)	24 months	24 months	52 months
Nowakowski *et al.*, (2015) [18].	Lenalidomide + R-CHOP	Lenalidomide: 25mg, Rituximab: 375mg/m^2, Cyclophosphamide: 750mg/m^2, Vincristine: 1.4mg/m^2, prednisone: 100mg	63 (98%)	51 (80%)	12 (18.7%)	70 months	37 months	23.5 months
Nowakowski *et al.*, (2011) [19].	Lenalidomide + R-CHOP	Lenalidomide: 25mg, Rituximab: 375mg/m^2, Cyclophosphamide: 750mg/m^2, Vincristine: 1.4mg/m^2, prednisone: 100mg	24 (100%)	19 (77%)	5 (20.8%)	NA	NA	7 months
Vitolo *et al.*, (2014) [20].	Lenalidomide + R-CHOP	Lenalidomide: 25mg, Rituximab: 375mg/m^2, Cyclophosphamide: 750mg/m^2, Vincristine: 1.4mg/m^2, prednisone: 40mg	45 (92%)	42 (86%)	3 (6%)	2 years=45	2 years=39	28 months
Chiappella *et al.*, (2013) [21].	Lenalidomide + R-CHOP	Lenalidomide: 25mg, Rituximab: 375mg/m^2, Cyclophosphamide: 750mg/m^2, Vincristine: 1.4mg/m^2, prednisone: 100mg	19 (90%)	17 (81%)	2 (9%)	NA	NA	<24 months

According to cumulative comparative effectiveness analysis, the Lenalidomide in combination with R-CHOP was a favourable choice in terms of overall response rate, complete response rate, however; partial response rate was better in Lenalidomide group as compared to Lenalidomide + R-CHOP as shown in (Figure 2).

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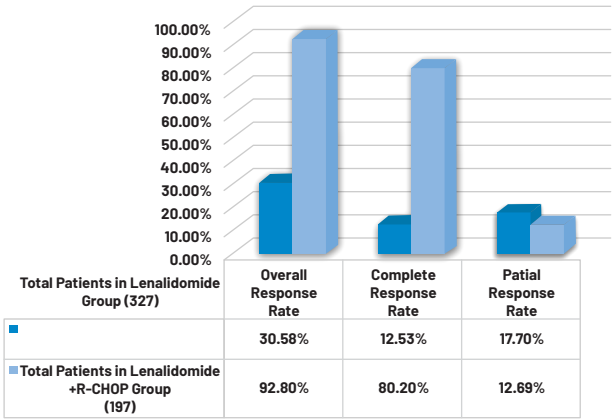


	Overall Response Rate	Complete Response Rate	Patial Response Rate
Total Patients in Lenalidomide Group (327)	30.58%	12.53%	17.70%
Total Patients in Lenalidomide +R-CHOP Group (197)	92.80%	80.20%	12.69%

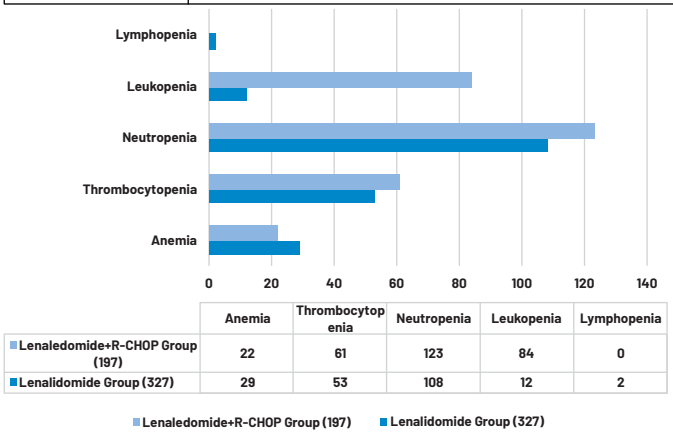
Figure 2: Showing the cumulative comparative effectiveness results of both Lenalidomide and Lenalidomide + R-CHOP study groups

b): Safety profile of Lenalidomide and Lenalidomide + R-CHOP study groups

In safety analysis between Lenalidomide and Lenalidomide + R-CHOP group, the combination therapy was associated with increased risk of Hematological and Non-hematological adverse events of grade 3 and more. The events of Hematological toxicities in both groups are given in the figure 3, which is clearly depicting the greater association of hematological toxicities with Lenalidomide + R-CHOP group as given in Table 6.

Table 6: Showing the safety profile of both Lenalidomide and Lenalidomide + R-CHOP study groups

Author Name (Lenalidomide)	≥ Grade 3 Hematological Toxicity N (%)	≥ Grade 3 Non-Hematological Toxicity N (%)
Mondello et al., (2016) [12]	Neutropenia=29(24%), Thrombocytopenia=13(11%)	Elevated transaminases=2(2%), Neuropathy=1(1%).
Witzig et al., (2011) [13].	Anemia=10 (9.2%), Neutropenia=44 (41%), Leukopenia=8 (7.3%), Thrombocytopenia=21(19.4%)	Dyspnoea=6 (5.5%), Abdominal pain=4 (4%), Pneumonia= 3 (3.3%), Deep venous thrombosis=2 (2.3%).
Wiernik et al., (2008) [14].	Anemia=2 (6.1%), Neutropenia=9 (33%), Leukopenia=4 (14.3%), Thrombocytopenia=5 (20%) Lymphopenia=1 (4%)	Fatigue=2(6.1%), Pain=1 (4%), Pneumonia=1 (4%), Rash=1 (4%), Fever=2 (6%)
Czuczman et al., (2017) [15].	Anemia=17 (33%), Neutropenia=22 (43%), Thrombocytopenia=12 (24%)	Respiratory dysfunction=28 (54%), Gastrointestinal dysfunction=37 (72%)
Beylot-Barry et al., (2019) [16].	Neutropenia=4 (21%), Thrombocytopenia=2 (10%) Lymphopenia=1 (5%)	Atrial fibrillation=3 (10.5%), Skin rash=1 (5%), Sepsis=1 (5%)
Author Name (Lenalidomide + R-CHOP)	**≥ Grade 3 Hematological Toxicity N (%)**	**≥ Grade 3 Non-Hematological Toxicity N (%)**
Sanjal et al., (2021) [17].	Neutropenia=27(82%), Thrombocytopenia=16(48%), Anemia=7(21%).	Fatigue=10(30.3%), Sensory neuropathy=4(12%), Alopecia=24(73%)
Nowakowski et al., (2015) [18].	Neutropenia=56 (87.5%), Leukopenia=51 (80%), Thrombocytopenia=28 (44%)	Fatigue=2 (3.1%), sepsis=1 (2%), Pneumonia=2 (3.1%).
Nowakowski et al., (2011) [19].	Anemia=5 (21%)	Infection=4 (17%), Neurological dysfunction=2 (8.3%), Vascular dysfunction=2 (8.3%).
Vitolo et al., (2014) [20].	Anemia=10 (20%), Neutropenia=34 (69%), Leukopenia=29 (59%), Thrombocytopenia=15 (30%)	Cardiac dysfunction=1 (2%), Cardiac dysfunction=2 (4%), Skin rash=1 (2%), Deep venous thrombosis=2 (4%)
Chiappella et al., (2013) [21].	Neutropenia=6 (28%), Thrombocytopenia=2 (9%), Leukopenia=4 (21%)	Cardiac dysfunction=2 (10%) Gastrointestinal dysfunction=1 (5%), Cardiac dysfunction=2 (10%)



	Anemia	Thrombocytopenia	Neutropenia	Leukopenia	Lymphopenia
Lenaledomide+R-CHOP Group (197)	22	61	123	84	0
Lenalidomide Group (327)	29	53	108	12	2

Lenaledomide+R-CHOP Group (197) Lenalidomide Group (327)

Figure 3: Showing the association of Hematological adverse events following Lenalidomide vs Lenalidomide + R-CHOP regimen

DISCUSSION

DLBCL is a complex illness with many subgroups that respond differently to treatment [22]. Despite conventional R-CHOP therapy, around one-third of DLBCL patients may have disease recurrence or progression, emphasizing the need for additional effective therapies [23]. Lenalidomide is an immunomodulatory medication that has been proven to be effective in DLBCL as a monotherapy as well as in combination therapy [24]. Several trials have investigated Lenalidomide monotherapy for relapsed or refractory DLBCL, with

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response rates varying between observed range of 24% to 36% [14, 18]. In a phase II trial of Lenalidomide in relapsed or refractory DLBCL, 25 patients were treated with Lenalidomide 25 mg/day on days 1-21 of a 28-day cycle [14]. The ORR was 36%, with a CR rate of 8%. The median PFS was 3.1 months, while the median overall survival (OS) was 7.3 months. In another phase II research of Lenalidomide in relapsed or refractory DLBCL, 46 patients were treated with Lenalidomide 25 mg/day on days 1-21 of a 28-day cycle [25]. The ORR was 24%, with a CR rate of 6.5%. The observed median PFS was 2.6 months, and the median OS was 7.6 months. According to these findings, Lenalidomide monotherapy shows limited effectiveness in relapsed or refractory DLBCL. These findings were consistent with our research findings, which showed that monotherapy was less successful than combination treatment. The ORR in our research was 30.58 %, with a CR rate of 12.53 %, which was comparable to other studies' findings. Several clinical trials have evaluated the efficacy and safety of Lenalidomide plus R-CHOP in newly diagnosed DLBCL [13]. In a phase II trial of Lenalidomide + R-CHOP in elderly individuals with DLBCL, 47 patients were given 15 mg/day of Lenalidomide plus R-CHOP on days 1-14 of a 21-day cycle [13]. The ORR was 93 %, with a 72 % CR rate. The two-year PFS was 75% and the two-year OS was 83%. In a phase II trial of Lenalidomide + R-CHOP in DLBCL, 59 patients were given 15 mg/day of Lenalidomide plus R-CHOP on days 1-14 of a 21-day cycle [20]. The ORR was 88%, with a CR rate of 56%, 2-year PFS was 61%, and the 2-year OS was 78%. In a phase III study of Lenalidomide plus R-CHOP in DLBCL, 233 patients were randomized to receive R-CHOP with or without Lenalidomide [26]. In this particular study, the ORR in Lenalidomide + R-CHOP was 66%, complete response 59% and partial response of 7%. These research findings corroborated what we had observed. The ORR in our trial for Lenalidomide + R-CHOP was 92.89 %, with a complete response of 80.20 % and a partial response of 12.69 %. The most prevalent type of aggressive NHL is DLBCL. Lenalidomide, an immunomodulatory medication, has been demonstrated to be effective as monotherapy in patients with recurrent or refractory DLBCL [27]. However, its safety in combination with R-CHOP is unknown. In a phase 3 clinical trial (ROBUST), the safety and efficacy of Lenalidomide plus R-CHOP in DLBCL patients were assessed. The study enrolled 818 patients who were randomly assigned to either R-CHOP + Lenalidomide (n=410) or R-CHOP plus placebo (n=408). The primary endpoint of event-free survival (EFS) was not attained, and there was no statistically significant difference in overall survival (OS) between the two groups. The addition of Lenalidomide, on the other hand, was linked with a higher incidence of grade 3 or 4 neutropenia (76.8 % vs 55.4 %), febrile neutropenia (13.3 % vs 7.1 %), and thrombocytopenia (15.3 % vs 7.1 %). In addition, the Lenalidomide group had a greater rate of treatment termination due to adverse events (23.2 % versus 12.0 %) [27]. Our research's safety trend was consistent with the previously described study, with neutropenia being the most often seen haematological toxicity, followed by thrombocytopenia. Another phase 2 trial investigated Lenalidomide in conjunction with R-CHOP in elderly individuals with untreated DLBCL [20]. The trial included 49 patients, and the findings revealed that the safety profile was good, with no paramount increase in side effects as compared to R-CHOP alone. Hematologic toxicity, particularly neutropenia and thrombocytopenia, was the most prevalent adverse event [20]. Finally, in DLBCL patients, the use of Lenalidomide with R-CHOP combination may increase the risk of hematologic toxicity and therapy abandonment due to adverse events. Careful monitoring and dosage modification may be necessary to reduce toxicity. Individual patient safety profiles for Lenalidomide + R-CHOP should be studied, taking the patient's age, comorbidities, and baseline hematologic characteristics into account.

CONCLUSIONS

DLBCL is an aggressive type of NHL. The two therapy options (Lenalidomide and Lenalidomide + R-CHOP) were compared in this study. In conclusion, the combination therapy was found to be successful in terms of greater ORR and CR, while the partial response rate was equivalent between the two groups. The safety profile revealed that combination therapy was associated with haematological and non-haematological side effects, most notably neutropenia and thrombocytopenia.

Authors Contribution

Conceptualization: MSA, SM, AR[1], AR[2]
Methodology: SY, MAKK
Formal Analysis: MF, MFB
Writing-review and editing: MSA, SM, AR[1], SY, MAKK, MF, MFB

All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

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