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ROBOTIC SURGERY - ECONOMIC IMPACT IN UNDERDEVELOPED COUNTRIES

Binafsha Manzoor Syed
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ABSTRACT

Robotic surgery also known as robot-assisted surgery is a type of minimally invasive surgery, which uses high technology computer system for surgical procedures. The robotic surgery is associated with high range of motion leading to high visibility resulting in low rate of per-operative complications and shorter hospital stay. Though it shows high success rate with low rate of complications but the cost of the robotic system and recurring cost is a challenge. The developing countries where basic health facilities are a challenge for government, installation of such high technology system may appear fancy without any great community benefit.

Key Words: Robotic surgery, Minimal invasive surgery, low middle income countries

INTRODUCTION

Robotic surgery, also known as robot-assisted surgery, is a type of minimally invasive surgery that utilizes robotic system to assist surgeons in performing surgical procedures. The primary goal of robotic surgery is to enhance the capabilities of surgeons, increased precision, flexibility, and control as compared to traditional surgical approaches.

The robotic surgery fundamentally involves use of a Robotic Surgical System, which typically consists of a console where the surgeon sits, a patient-side cart with robotic arms, and a high-definition 3D vision system. The surgeon controls the robotic arms from the console, manipulating specialized instruments with precision. The robotic arms hold and manipulate surgical instruments. These arms can mimic the hand movements of the surgeon in the conventional system with a high degree of precision and a range of motion. Specialized instruments are attached to the robotic arms. These instruments can be interchangeable and tailored for different types of surgeries. The commonly used tools include those used for cutting, suturing, and cauterizing tissues. The system also provides the surgeon with a high definition three-dimensional view of the surgical site. This enhanced visualization helps the surgeon to navigate complex anatomical structures with greater accuracy, thus reducing the risk of per-operative complications.

BENEFITS OF ROBOTIC SURGERY

The robotic system allows for precise movements with reduced hand tremors, enabling delicate procedures in confined spaces. Robotic surgery is often performed through small incisions, leading to less scarring, reduced pain, and faster recovery as compared to conventional open surgery. The 3D vision system provides a detailed view of the surgical site, allowing for better identification of structures and improved decision-making. Thus in general lesser risk of damage to the surrounding

structures. It can be used for a wide range of procedure including but not limited to urological, gynaecological and biliary surgeries.

LIMITATIONS OF ROBOTIC SURGERY

As mentioned earlier robotic surgery has many benefits but it is also associated with a number of limitations, where the cost of equipment and the need for specialized trained staff to operate the robotic system are the major challenges. The equipment installation involves huge amount of investment, then there is the maintenance cost further adds to the recurring cost. Moreover, the trained staff can manage the equipment properly otherwise mishandling of the system can lead to further cost of repair and potential harm to the patient.

ECONOMIC IMPACT OF ROBOTIC SURGERY IN UNDERDEVELOPED COUNTRIES

The economic impact of robotic surgery in underdeveloped countries is a complex and multifaceted issue. While robotic surgery offers potential benefits, it also comes with challenges that may limit its widespread adoption in resource-constrained settings. On one hand shorter hospital stay, fewer complications and faster recovery save cost of each surgical procedure. The high initial cost is a significant barrier for underdeveloped countries with limited healthcare budgets. In addition training healthcare professionals to use and maintain the technology can be resource-intensive and may be challenging in regions with limited access to education and training facilities. From perspective of Pakistan, where there are limitations of infrastructure and basic healthcare facilities in many regions, installation of robotic surgery would not be a great idea to handle. As the system required constant power supply and high speed internet which is again a challenge in limited resource countries. In limited resource countries it raises an ethical issue for the decision makers that where they prioritize primary and basic health care system to improve needs such as immunization, maternal care, and infectious disease control, then investing in advanced surgical technology. One the other hand developing countries may attract patients from other regions seeking advanced medical treatments. This could potentially boost the healthcare sector and generate revenue. The implementation of robotic surgery may create job opportunities in various sectors, including healthcare, technology, and support services. This could have a positive impact on employment rates. Collaborations with international manufacturers of robotic surgical systems could facilitate technology transfer and promote innovation within the country. This, in turn, may boost the technological sector and foster research and development.

CONCLUSION

In summary, it is multifactorial to make a decision of introducing robotic surgery in a limited resource country where risk and benefits may be compared with great care. However, it may further compromise the budget spent on provision of basic health facilities. Thus may raise an ethical issue.

Research article

EARLY SURGICAL COMPLICATIONS IN KIDNEY TRANSPLANT RECIPIENTS - A SINGLE CENTRE STUDY

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ABSTRACT

End-stage renal disease (ESRD) is becoming a significant global public health issue. The preferred course of treatment for people with ESRD is kidney transplantation, although its associated surgical complications raise serious doubts about the success rate of the procedure. Renal transplant surgical complications are frequently observed and can significantly affect graft performance, survival, and patient morbidity. This study aimed to analyze the frequency of early surgical complications, diagnoses, and treatment options in renal transplant patients. This retrospective cohort study included all transplanted patients with surgical complications from April 2017 to April 2022 at the Renal Transplant Unit of the Dow University of Health Sciences, Karachi, Pakistan. Out of 500 kidney transplant recipients, 86 patients (17.2%) experienced early post-transplant surgical complications. The most common complication was Lymphorrea (n=38, 7.6%) followed by wound infection (n=25 patients, 5%). The occurrence of these complications was associated with delayed graft function, indicating the need for careful monitoring and timely intervention in these cases. Future studies are needed to explore the predictors and risk factors of surgical complications in kidney transplantation and to identify strategies for reducing the incidence and improving the outcomes of these complications.

Key Words: Kidney transplantation, early post-transplant surgical complications, lymphocele, wound infection

INTRODUCTION

Chronic renal failure is a devastating ailment and the number of cases are increasing globally with the rise in the chronic diseases such as diabetes and hypertension. Its effects are greater in economically underdeveloped third-world countries, where the majority of patients and their families are unable to access, or afford renal replacement treatments. Kidney transplantation is a life-saving treatment for end-stage renal disease (ESRD) patients, who are on dialysis or have severe kidney dysfunction. It has become the preferred treatment option over the years due to its superior outcomes, including better quality of life, reduced morbidity and mortality(1), and lower healthcare cost (2,3). However, kidney transplantation is not completely risk free, it is associated with post-transplant surgical complications. These surgical complications may result in graft loss, delayed graft failure, patient morbidity, and even death(4). The initial post-transplant period is a critical time when patients are at a high risk of developing surgical complications, which can significantly affect their outcomes(4). The rate of surgical complications after renal transplant vary from 4.2% to 34%, depending the region of the reporting center (5,6).

RENAL TRANSPLANTATION TECHNIQUE:

Our kidney transplant program is a live- related program, which means all donors are live- related. A single team of surgeons conducts all of the transplants, using standard surgical techniques for kidney transplantation(7). Donor nephrectomy is performed by an open surgical method using a flank incision, and the graft is perfused

with custodial solution. Bench dissection is then carried out to prepare the graft for anastomosis. The majority of kidneys are placed in the right iliac fossa using an extra-peritoneal approach. However, if the iliac vessels are blocked on the right side due to history of femoral catheterization, the kidney is placed in the left iliac fossa(8). The graft vessels are anastomosed with external or common iliac vessels by end-to-side method. In cases where there are multiple arteries in the allograft, they are either dealt with separately or made double barrel before anastomosis to the recipient vessel. Proline 6/0 is used for fine suturing of the anastomosis. For ureteric anastomosis, standard leich-gregoid techniques are used in all cases. A double J stent is placed in the majority of patients during ureteric anastomosis, which is removed after 2-4 weeks. All recipients are given broad-spectrum antibiotic prophylaxis before induction, but anti-coagulant therapy is not used routinely post-operatively unless there is some medically or surgically indicated reason(9).

After surgery, kidney transplant patients are shifted to the surgical ICU for close clinical and biochemical monitoring. Routine color Doppler ultrasound is performed on the first post- operative day, but in case of emergency, it can be done per-operatively or immediately after surgery to check graft perfusion and any collection. Per-operative surgical complications are dealt with accordingly, while post-operative surgical complications are dealt with as emergencies. For immediate post-operative vascular complications, color Doppler studies, CT with contrast, and MRI are performed to confirm the diagnosis. Other surgical complications like Lymphorrea and wound-related issues are diagnosed clinically(10).

After being discharged, patients are followed up in the Out Patient Department (OPD) initially on a weekly basis for one month, then biweekly the next month, and then after three months for one year. During each visit, routine blood tests and urine DR are done, and ultrasound and color Doppler are only done if clinically indicated. The most frequently used immune-suppression medications are cyclosporine, tacrolimus, mycophenolate, and prednisolone(11).

EARLY POST TRANSPLANT SURGICAL COMPLICATIONS:

Kidney transplant surgical complications can be classified into urological, vascular, wound related and others.

UROLOGICAL COMPLICATIONS:

Common urologic complications following kidney transplantation may affect patient graft function, survival, and morbidity. In the literature, the incidence of urologic complications ranges from 3.4% to 11.2%(12–21). Urine leak, ureteral stricture, DJ stent encrustation or misplacement, urolithiasis, obstruction of the bladder outlet, and bladder rupture are reported complications. Urinary leak is a common complication that can occur due to faulty anastomosis or damage to the ureter during surgery. Leakage of urine from the site of anastomosis or from the ureter can occur, requiring additional surgical intervention. Urinary obstruction can occur due to blood clots, swelling, or scar tissue formation, while DJ stent Encrustation can happen naturally as a result of high amounts of certain minerals in the urine (such as calcium, oxalate, and phosphorus), or it can be triggered by the presence of urease-producing organisms, which can result in urolithiasis formation. Bladder injury is iatrogenic complication but patients rarely experience bladder injury during renal transplantation.

VASCULAR COMPLICATIONS:

Vascular complications account for 3% to 15% of all cases and are usually associated with graft loss(22). Vascular complications following kidney transplantation can occur in the form of renal artery stenosis, renal vein thrombosis, bleeding, or aneurysm of the renal artery. Renal artery stenosis is the narrowing of the artery that supplies blood to the transplanted kidney, which can lead to decreased kidney function. Renal artery and vein thrombosis occur when a blood clot blocks the blood vessels, which can result in decreased blood flow to the transplanted kidney. Bleeding can occur due to surgical complications or anticoagulation therapy, while aneurysm of the renal artery is a rare complication that can occur due to weakening of the artery wall.

HAEMORRHAGIC COMPLICATION:

Any bleeding associated with a surgical transplant process that required additional intervention, aspiration, or blood transfusion was referred to as a post-operative bleeding complication. Incidence rates of bleeding after kidney transplantation surgery has been reported as around 12% (23).

WOUND RELATED COMPLICATIONS:

Wound complications are indeed common after kidney transplantation, incidence of surgical wound infection range from 2% to 26% of patients(24,25). They can be categorized into superficial and deep wound complications, each with its own characteristics.

1. **Superficial Wound Complications:**

Superficial wound infections can occur as a result of bacterial contamination during or after the surgery. These infections may manifest as redness, swelling, warmth, pain, or drainage from the wound site. Wound dehiscence refers to the partial or complete separation of the wound edges. It can be caused by factors such as poor wound closure technique, excessive tension on the incision, or infection. Seroma is the accumulation of fluid in the wound area, resulting in swelling and a fluid-filled cavity. It can occur due to disrupted lymphatic drainage or inadequate closure of the wound layers.

2. **Deep Wound Complications:**

Any wound that required a second treatment to close it and had an infection that reached the facial and musculature layers is labelled as a deep wound.

- *Hematoma:* A hematoma is a collection of blood within the wound or surrounding tissues. It can occur due to bleeding from blood vessels during the surgery or as a result of clot formation.
- *Abscess Formation:* An abscess is a localized collection of pus within the wound or surrounding tissues. It can occur due to infection and can present with symptoms such as pain, swelling, and fever.
- *Wound Breakdown:* Wound breakdown refers to the complete disruption of the wound, resulting in an open wound. It can occur due to factors such as poor wound healing, infection, or excessive pressure on the incision site.

Despite efforts to minimize surgical wound complication through improved surgical techniques, perioperative antibiotics, targeted therapy and optimized immunosuppression, these wound complication remain a major clinical challenges(26–28). These wound complications can cause discomfort, delay healing, prolong hospital stays, and increased risk of other complications. Proper wound care, including regular monitoring, infection prevention measures, and timely intervention, is crucial to manage these complications effectively.

LYMPHATIC COMPLICATION:

A *lymphocele* is an accumulation of lymph around the graft. It usually appears within the first six months following the transplant, increasing at six weeks. Depending on the series, the mean incidence of lymphocele varies between 0.5% and 20%(29). *Lymphorrhea* is the prolong drainage of fluid after transplant and cause morbidity and long hospital stay. Risk factors include age, BMI, fluid overload, hemodialysis period, diabetes, acute rejection, use of steroids and diuretics and coagulopathy(30–34).

OTHERS COMPLICATIONS:

Gastrointestinal injury: Intestinal perforation is a rare but serious complication that can occur during or after kidney transplantation. It is estimated to occur in about 1% to 2% of patients according to various reports(35). This complication can occur due to various factors, including surgical trauma to the intestines, vascular compromise leading to ischemia.

GRAFT LOSS:

Early graft loss defined as graft loss occurring within 30 days after kidney transplantation, is relatively uncommon and occurs in approximately 5% of kidney transplants(36). However, it is a physically and emotionally devastating outcome for both the recipient and the transplant team. Despite advancements in transplantation techniques and immunosuppressive medications, graft loss can occur due to various factors. These factors may include medical and surgical factors, medical factors include acute rejection, chronic rejection, infections, while surgical factor include vascular complications. Prompt identification and management of the underlying causes are crucial in minimizing the risk of graft loss and preserving the long-term success of kidney transplantation.

MANAGEMENT OF EARLY POST TRANSPLANT COMPLICATIONS:

Early recognition and prompt management of surgical complications are critical in improving outcomes and reducing morbidity and mortality. Failure to identify and manage surgical complications can lead to graft dysfunction, loss of the transplanted kidney, and even death. Therefore, close monitoring and prompt interventions are essential during the post-transplant period.

Management of Urological Complications:

Urinary Leak: This complication is typically managed conservatively through measures like bed rest, bladder drainage, and urinary diversion using a urethral catheter or percutaneous nephrostomy. Severe cases might necessitate surgical intervention or open repair of the ureter.

Urinary Obstruction: Management involves stent placement or percutaneous nephrostomy tube insertion to alleviate the obstruction. If these methods fail, surgical intervention, such as revision or re-implantation of the ureter, may be required.

DJ Stent Obstruction: This is managed by either removing and replacing the stent or repositioning it using a cystoscope.

Bladder Rupture: Urgent surgical intervention is typically necessary, involving repair or reconstruction of the bladder.

Management of Vascular Complications:

Renal Artery Stenosis: Managed through angioplasty and stent placement. If unsuccessful, surgical intervention like renal artery bypass grafting might be needed.

Renal Vein Thrombosis: Managed by surgical exploration.

Bleeding: Management includes blood transfusions and/or surgical intervention, such as vascular repair or embolization.

Management of Wound Complications:

Superficial Wounds: Managed with wound care, including daily dressing changes or wound irrigation. Antibiotic therapy may be necessary in some cases.

Deep Wounds: May require surgical intervention like debridement, drainage, and wound closure. Antibiotic therapy might also be needed.

Management of Fluid Collection Complications:

Lymphocele/Lymphorrhea: Conservative management involves pyodine or ethanol instillation. If unsuccessful, surgical intervention like laparoscopic or open drainage might be considered.

Hematoma: Managed with observation and monitoring for bleeding or infection signs. Surgical intervention, such as drainage or hematoma evacuation, may be required in certain cases.

Management of Gastrointestinal Injury Complications:

Managed through surgical intervention, including repair or reconstruction of the injured gastrointestinal tract. Antibiotics and supportive care are provided for associated complications like sepsis.

This retrospective study aimed to evaluate the rate and types of surgical complications within the first month after kidney transplantation, as well as their impact on graft and patient outcomes. The study also attempted to identify the risk factors associated with surgical complications to help guide clinicians in identifying patients who are at a high risk of developing surgical complications and instituting appropriate preventive measures.

METHODS

This retrospective cohort study was conducted at the Renal Transplant Unit of Dow University of Health Sciences, Ojha campus, Karachi, Pakistan. The study included all patients who had undergone kidney transplantation and experienced surgical complications between April 2017 and April 2022. The sample size was 500 determined by the number of patients who had a kidney transplantation. All transplanted patients were included while pediatric patients, second transplants, transplants in augmented bladders, and positive cross match transplants were not included in the study.

Data were collected from the medical records of patients who had undergone kidney transplantation and experienced surgical complications. A standardized checklist was used to collect information on patient age, gender, and descriptions of the surgical complications, diagnosis, and their management. The medical records of patients who met the inclusion criteria were reviewed, and the data were extracted from the system of Renal Transplant Unit of Dow University of Health Sciences.

Ethical clearance was obtained from the Institutional Review Board (IRB) of Dow University of Health Sciences. The findings of this study will contribute to the body of knowledge on early post-transplant surgical complications among kidney recipients, which may ultimately lead to improved patient outcomes and better-informed decision-making by healthcare professionals.

Statistical analysis

All statistical analyses were performed using the Statistical Package for the Social Sciences(SPSS) version 20.0. Descriptive statistics were calculated to present the basic demographic characteristics of the study population, including the mean, standard deviation (±SD), and range for continuous variables, and the frequency and proportion for categorical variables. The relationship between the demographic and clinical characteristics of the study population and the incidence of post-transplant surgical complications was evaluated using the chi-square test for categorical data. A P-value of <0.05 was considered statistically significant.

RESULTS

Majority of the kidney transplant patients in the study were males (70.9%) and aged between 21 to 50 years. The most common blood group among the patients was A+ (44.1%) and the majority had a Body Mass Index (BMI) within the normal range (67.4%). A summary is given in Table 1. In terms of residence, most of the patients were from Sindh (43.0%) and 38.4% were married. In terms of occupation, the most common occupation among the patients was being a businessman (25.5%) or unemployed (23.2%), and most patients belonged to the upper class (51.1%).

Most frequent cause of renal failure was hypertension, accounting for 32 (37.2%) cases, followed by diabetes mellitus identified in 28 (32.6%) cases, whereas, 26(30.2%) cases had both comorbid conditions, hypertension and diabetes mellitus (Figure 1).

Out of 500 kidney transplant recipients, 86 patients (17.2%) experienced early post-transplant surgical complications. The most common urological complications were urinary leak (n= 5 cases) and DJ stent encrustation (n= 3 cases). Vascular complications included renal artery stenosis (n=1 case), renal vein thrombosis (n=1 case), and bleeding (n=2 cases). Wound complications were observed in 25(5%) of cases, with 20 cases of superficial wound complications and 5 cases of deep wound complications. Prolong Fluid drainage (Lymphorrhea) were observed in 38(7.6%) cases, out of which 30 patients were treated conservatively at bed side with pyodine or ethanol and only 5 cases needed exploration. Hematomas were observed in 5 patients out of which 2 patients were treated conservatively and 3 patients need re-exploration and drainage of hematoma. Gastrointestinal injury occurred in 1 case, and graft loss was observed in 1 case (Table 2). Out of the 500 patients, only 1 patient died within the study period, resulting in a 0.2% mortality. The cause of death were graft loss in this patient.

DISCUSSION

Our study presented a low rate of complications in patients undergoing renal transplant, whereas only 0.2% of mortality. Previously reported studies such as study by Berhe and another study by Salamin et al, reported a 26% and 34.9% respectively, which is a little higher than the rate reported in our study(37,38). The Berhe et al reported data from Ethiopian transplant recipients, while Salamin et al. Swiss patients experienced complications within the first year of transplantation. This suggests that surgical complications are a significant issue globally, regardless of the setting.

The types of surgical complications reported in our study were similar to those reported in the other studies, including urologic complications, vascular complications, and wound-related complications. Choate et al. and Ammi et al. reported urologic complications to be the most common type of surgical complications in kidney

transplant recipients, while vascular complications were the second most common complication reported in the study by Ammi et al(39,40). In contrast, our study found Lymphorrea (7.6%) to be the most common type of surgical complication, wound-related complications were the second most common early post - transplant surgical complication. This difference could be due to the differences in the characteristics of the study population which can significantly influence the outcomes. Factors such as age, comorbidities, immunosuppressive regimens, and surgical techniques can vary across studies and contribute to variations in complication rates.

Table 1. Socio-demographic characteristics of kidney transplant patients developed complications

Characteristics	N (%)
Age in years	
<20	10(11.6)
21-30	30(34.9)
31-40	21(24.4)
41-50	25(29.0)
Gender	
Males	61(70.9)
Females	25(29.1)
Blood group	
A (+ve)	38(44.1)
B (+ve)	19(22.0)
AB (+ve)	29(33.7)
Body Mass Index (BMI)	
18.1-25	58(67.4)
>25	28(32.5)

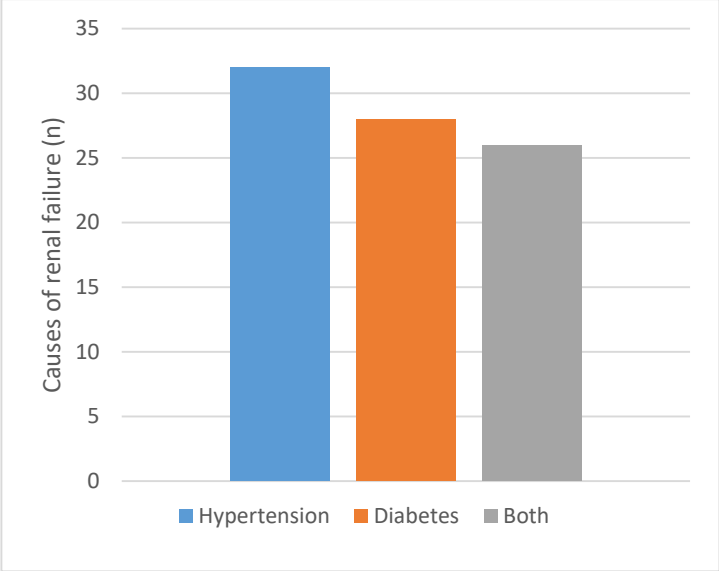
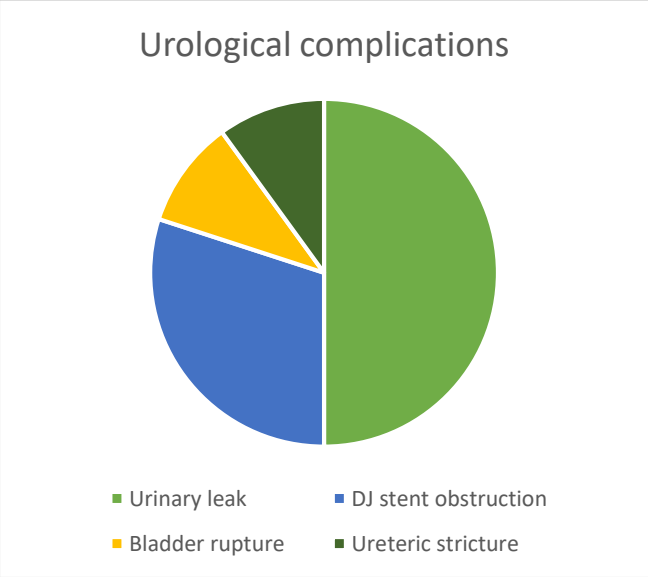
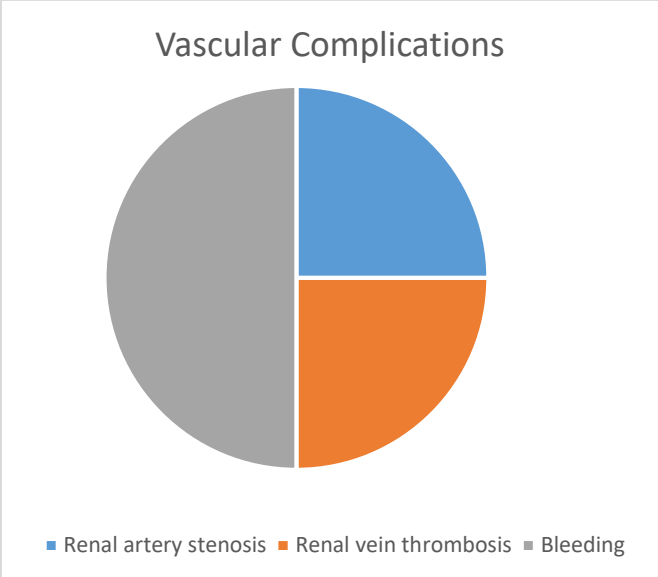
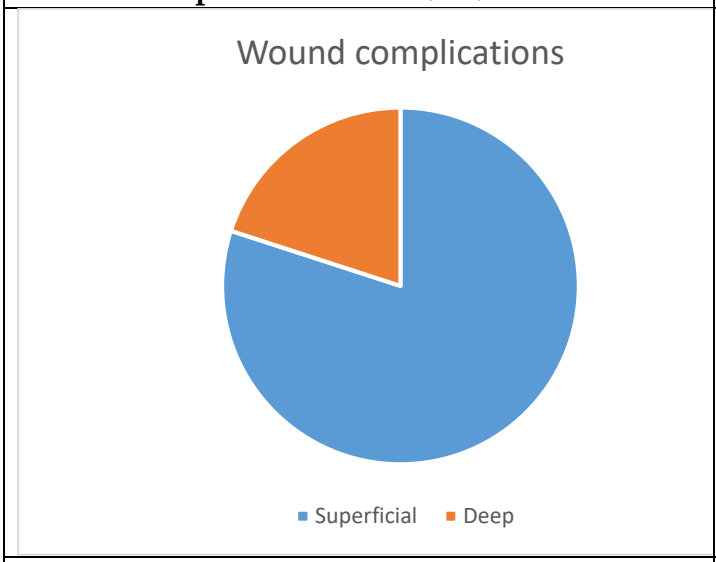
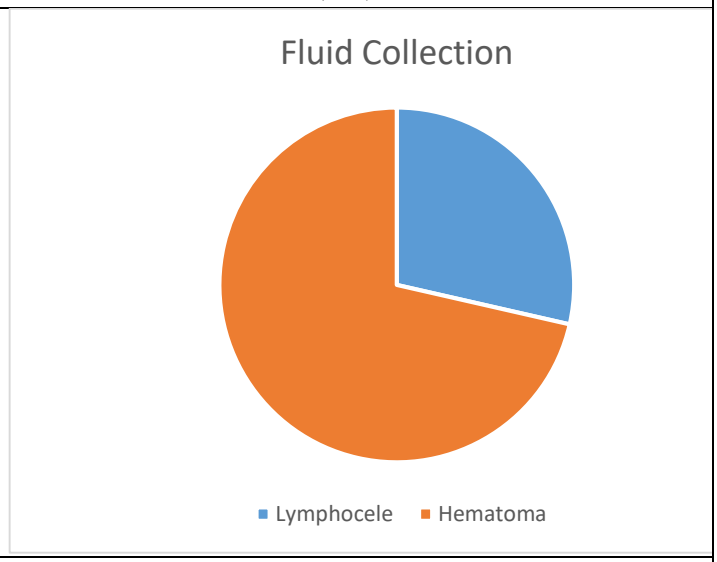


Figure 1. Causes of renal failure in patients underwent renal transplant and developed post-operative complications

Table 2. Summary of surgical complications in patients undergoing renal transplant and developed surgical complications

Urological complications n= 10 (2.0%)	Vascular Complications n=4 (0.8%)
	

Wound complications n=25 (5%)	Fluid Collection n=7 (1.4)
	
Lymphorrhea n=38 (7.6%)	**Gastrointestinal injury n=1 (0.2%)**
Graft loss n=1 (0.2%)	

The severity of the surgical complications in our study was also comparable to that reported in the other studies. Carvalho et al reported that the most severe complications were due to vascular and urologic issues, while Sugi et al reported that complications ranged from mild to life-threatening(41,42). Similarly, in our study, the majority of the complications were mild, with only one patients experiencing severe complication. This suggests that while surgical complications are common in kidney transplant recipients, the severity of the complications varies depending on the type and management.

In terms of risk factors for surgical complications, the findings of the studies were somewhat consistent. Salamin et al identified several risk factors, including recipient age, recipient BMI, and donor type, which were also identified as risk factors in our study(38). Hamed et al and Szabo-Pap et al reported that cold ischemia time and donor age were significant risk factors for surgical complications, while Bejic et al found that the use of intraoperative duplex ultrasound reduced complications in living renal donor transplantation(43–45).

Overall, the findings from our study are consistent with those of the other studies in terms of the prevalence, types, and severity of surgical complications in kidney transplant recipients. However, there were some differences in the types and order of the most common complications reported. Further research is needed to identify additional risk factors and determine the most effective strategies for managing and preventing surgical complications in kidney transplant recipients.

Our study is the largest study from the region presenting data from a single centre with five years follow-up, however the study only focused on the surgical complications and outcomes of kidney transplantation which is considered as limitation of the study.

CONCLUSION

The study reported overall low rate of surgical complications was relatively mild, suggesting that while complications were present, but they were not excessively high in frequency. However, the study also found that the overall graft and patient survival rates were relatively good, which underscores the importance of establishing transplant programs in developing countries to address the growing burden of end-stage renal disease. Future studies are needed to explore the predictors and risk factors of surgical complications in kidney transplantation and to identify strategies for reducing the incidence and improving the outcomes of these complications.

CONFLICT OF INTEREST:

Authors declare no conflict of interest

FUNDING SOURCE:

The study did not receive any external funding

ETHICAL APPROVAL:

The data was retrospective analysis of hospital record, did not require ethical approval. At the time of transplant informed consent, patients and donors also consent for utilization of their information for research purpose.

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Research Article

EFFECTS OF SMOKELESS TOBACCO ON THE UTERINE WALL OF ADULT NON PREGNANT FEMALE SWISS ALBINO RATS

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ABSTRACT

This study was aimed to evaluated effects of smokeless tobacco on the uterine wall of female rats of Swiss albino species. This was a controlled experimental study with three groups of adult female Swiss albino rats. The study was conducted over a period of 31 days, at Animal House, Husbandry, and Veterinary Sciences at Sindh Agricultural University, Tandojam, and the Department of Anatomy, Isra University, Faculty of Medicine & Allied Medical Sciences, Hyderabad, Sindh, Pakistan. Thirty adult female Swiss albino rats were randomly assigned to three groups: Group A (control, no treatment), Group B (treated with 5% smokeless tobacco), and Group C (treated with 10% smokeless tobacco). Blood samples were collected on the 31st day to analyze Follicle-stimulating hormone (FSH) and Luteinizing hormone (LH) levels in the serum. After euthanization, uteruses were removed and weighed, followed by histological examination using Hematoxylin & Eosin and Mason's trichrome stains. The experimental groups (B and C) exhibited a significant reduction in uterine weight and decreased serum levels of FSH & LH. Histological examination showed cystically dilated submucosal glands and pronounced atrophy in the uteri of the experimental groups. Additionally, the myometrial wall thickness was also decreased. The use of smokeless tobacco negatively affects the uterine wall of female Swiss albino rats, resulting in histological changes and decreased serum levels of FSH and LH.

Key Words: Serum FSH, Serum LH, Smokeless Tobacco, Swiss Albino Rats, Urogenital Diseases, Uterine wall

INTRODUCTION

Smokeless tobacco is a popular form of tobacco consumed in many countries, particularly in South Asia. Tobacco is known for its harmful impact on human health, causing various diseases such as cancer, cardiovascular diseases, and respiratory disorders. Despite the well-established negative impact on health, the use of smokeless tobacco is still prevalent in many countries of the world(1). Recently, researchers have expressed concern regarding the effects of smokeless tobacco on female reproductive health. Smokeless tobacco contains several toxic substances, such as nicotine, polycyclic aromatic hydrocarbons, and nitrosamines. These substances have potentially detrimental effects on the female reproductive system. Earlier studies have shown that smokeless tobacco use during pregnancy can lead to adverse outcomes, including preterm delivery, stillbirths, and low birth weight (2).

Nevertheless, the impact of smokeless tobacco on the uterine wall of adult non-pregnant female rats has not been extensively studied (3). The uterine wall is a vital component of the female reproductive system, and any

disruption to its function can lead to significant reproductive problems(4). Therefore, this study aimed to investigate the impact of tobacco (smokeless) on the uterine wall of adult non-pregnant Swiss female albino rats. Gaining insights into the reproductive health implications of smokeless tobacco use in females can be significantly enhanced by comprehending the effects of smokeless tobacco on the uterine wall of non-pregnant female rats(5). The results of this study may add to the development of interventions and formulate strategies to reduce the use of smokeless tobacco and its harmful impact on female reproductive health.

METHODS

The research was jointly conducted at two locations: The Animal House, Husbandry, and Veterinary Sciences at Sindh Agricultural University, Tandojam, Pakistan and the Department of Anatomy, Isra University, Faculty of Medicine & Allied Medical Sciences, Hyderabad, Sindh, Pakistan. The study involved a total of thirty female adult Swiss albino rats, randomly selected and divided into three groups, each consisting of 10 rats. Group A served as the control group, while groups B and C were administered 5% and 10% smokeless tobacco, respectively, in their feed.

Throughout the study, the rats had unrestricted access to both feed and water for a duration of one month. On the 31st day, blood samples were collected from the animals' tails in each group to assess the levels of serum follicle-stimulating hormone (FSH) and luteinizing hormone (LH). Subsequently, the rats were humanely euthanized by cervical dislocation, and their uteri were removed and weighed. The uterine tissues were then processed and subjected to histological examination by making Paraffin blocks after dehydration, cleaning, and infiltration of the samples. Tissues were sectioned to a thickness of 5 micron using a microtome and placed under water bath. Then slides were prepared and stained using Hematoxylin and Eosin stain and studied under light microscope. Masson's Trichrome stain was used to differentiate collagen and muscle fibers on tissue sections.

STATISTICAL METHODS

Data analysis was performed using Statistical Package for Social Sciences (SPSS version 22.0), with measures of central tendency employed, and Student's t-test and ANOVA were used to compare the study groups. A p-value <0.05 was considered significant.

RESULTS

A total of 30 rats were used; 10 in each group (A, B and C). The mean weight of the uterus in Group A was 1.115 ± 0.005, while in Group B, it was 0.596 ± 0.009 (p-value <0.001). There was a significant difference in Group A and C (p-value <0.001). Group A exhibited a mean uterus weight of 1.115 ± 0.005, significantly higher than Group C with a mean weight of 0.459 ± 0.011. The FSH and LH levels of all three goups was compared and there was significantly higher concentration of hormones found in Group A while lowest was obseved in Group C (p-value <0.001). The histological presentation of the endometrial glands of uterus removed from Group A is presented in Figure 1, the endometrium and the stroma appears normal while Figure 2 presents uterus removed from Group C, which illustrated severe cystically dilated submucosal glands with marked atrophy in this group. Furthermore, there was a reduced thickness of the myometrial wall, with atrophic changes observed under H&E staining. Additionally, trichrome staining indicated pronounced fibrosis in both the endometrium and myometrium (Figure 3).

Table 1: Comparison of weight of uterus of Swiss albino rats: Control Group (A) versus 5% somkeless tobacco Group (B) and 10% smokeless tobacco Group (C)

Group	Mean ± SD	p- value
Group A versus B		
A	1.115± 0.005	<0.001
B	0.596 ± 0.009	
Group A versus C		
A	1.115± 0.005	
C	0.459 ± 0.011	

Table 2. Comparison of follicle stimulaing hormone and Letuinizing Hormone hormonal levels between Group A, B and Group causing ANOVA test where n=10/group

Group	Follicle Stimulating Hormone Mean ± SD	Luteinizing Hormone Mean ± SD	p- value
A	21.92 ± 2.95	6.12 ± 1.3	**<0.001**
B	16.01 ± 1.22	3.32 ± 0.12	
C	14.03 ± 1.18	2.80 ±0.15	

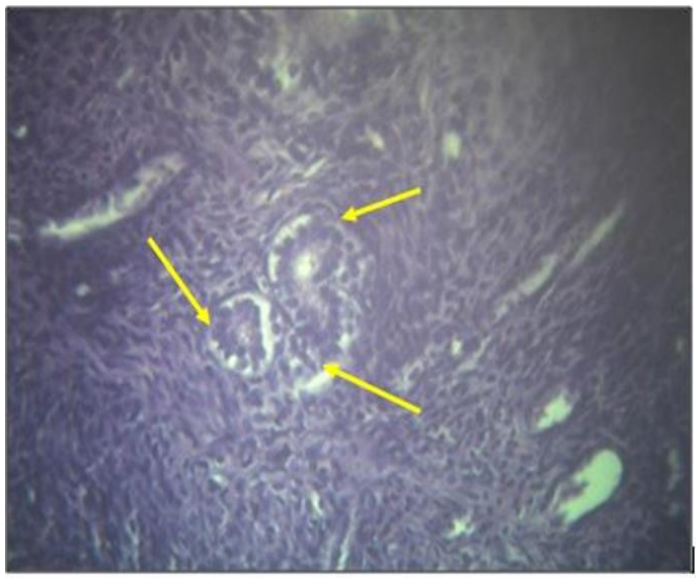

Figure 1. Uterus of group A where the arrowheads indicate healthy endometrial glands x 10

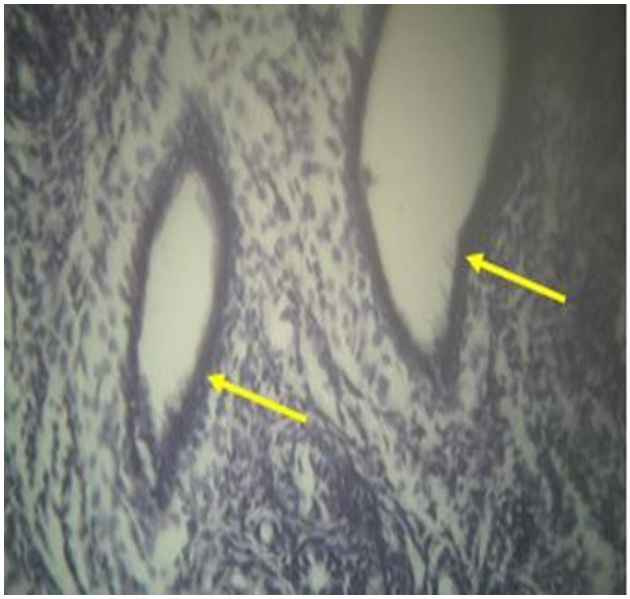

Figure 2. Uterus of group C where the arrowheads indicate cystically dilated endometrial glands x 40

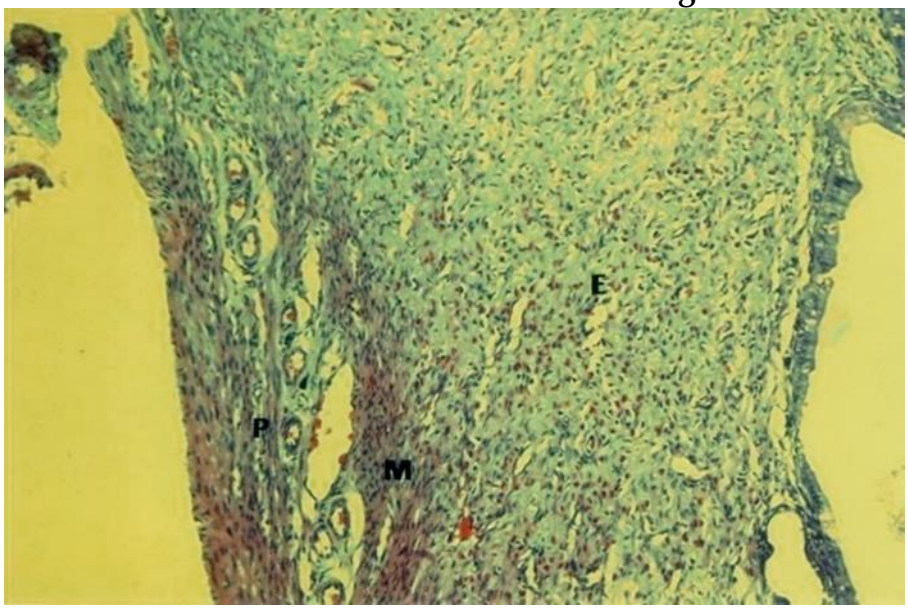

Figure 3. Uterus of group C where E, M & P indicate endometrium, myometrium & perimetrium respectively under Mason's Trichrome staining x 40

DISCUSSION

The periodic secretion of pituitary gonadotrophins, such as FSH and LH, is regulated by the hypothalamus and prolactin, through neural stimulus to Gonadotropin-releasing hormone (GnRH). Nicotine, a central nervous system influencing agent found in tobacco, has been shown to inhibit the release of gonadotrophins from the pituitary gland, leading to dysregulation of the reproductive hormonal system in both healthy women and animals (6). In the context of this study, estrogen plays a crucial role in uterine growth, primarily affecting the surface epithelium and endometrial glands. Subsequently, progesterone prepares the uterine epithelium, transitioning it from a proliferative to a secretory state. Moreover, the study revealed a decrease in serum concentrations of FSH and LH hormones, indicating inhibition of ovarian steroid biosynthesis, which is indispensable for uterine development and reproductive cyclicity(7).

The present research demonstrated that consumption of smokeless tobacco resulted in endometrial degeneration, fibrosis, and edema. The uterus of the tobacco-treated rats exhibited necrosis, cystic dilatation, and atrophy in the endometrial glands. These results were in agreement with the preceding study, which also found a noticeable decrease in the thickness of both the endometrium and the endometrial glands in rats receiving nicotine administration(6). Moreover, toxins constituting tobacco can also impede the receptivity of the endometrial, uterine blood flow, and endometrial angiogenesis. The findings from the current study, which include a diminished endometrial thickness and reduced size of endometrial glands, suggest the inhibition of ovarian steroid biosynthesis. These hormones are crucial for uterine growth and reproductive activity(7,8). The present study provides evidence that the consumption of smokeless tobacco causes dysregulation of the reproductive hormonal system and impairs uterine growth through endometrial degeneration, edema, and fibrosis. These findings are consistent with the above studies and highlight the harmful effects of tobacco use on the health of the female reproductive system as previously reported(7).

One study that investigated the weight of the uterus in Pakistani women measured the weight of the uterus in 126 women who underwent hysterectomy for benign conditions(9). The mean weight of the uterus was 82.7 ± 45.1 grams. The study found no substantial changes in the weight of the uterus between women of different age groups or parity(9).

Another study conducted by Octaviana et al. examined hormonal levels in 100 women with irregular menstrual cycles. They measured estrogen, progesterone, and follicle-stimulating hormone levels and identified notable distinctions in these hormone levels among women with varying menstrual patterns(10). The present study validated that the consumption of smokeless tobacco in rats led to myometrial degeneration along with fibrosis and edema. This is in agreement with previous studies, such as the study by Khorram et al. (2010), which showed a significant reduction in the thickness of the uterine wall, particularly in the myometrium, in response to smokeless tobacco exposure(11). Another study also demonstrated that smokeless tobacco compounds were capable of altering the endometrial strata and myometrium. These findings suggest that smokeless tobacco use can have significant impacts on the structure and function of the uterus.

Moreover, smokeless tobacco has been known to lead to stromal inflammation and cellular edema, which can further exacerbate the damage to the uterus(12). The findings of the current study align with this observation, as it also demonstrated that the administration of smokeless tobacco to rats resulted in compromised endometrial receptivity and angiogenesis. These results highlight the

potential hazards of smokeless tobacco use on reproductive health and suggest that women who use smokeless tobacco may be at increased risk for infertility and other reproductive disorders(13).
Previous studies have shown that the effects of tobacco use on the reproductive system are similar in animals (rats) and humans. Therefore, it is essential to further investigate the potential impacts of smokeless tobacco use on reproductive health in human population.
This study provides evidence that the use of smokeless tobacco can have significant impact on the structure and function of the uterus, leading to myometrial degeneration, fibrosis, and edema. These findings underscore the need for increased public health efforts to educate women on the potential dangers of smokeless tobacco use and to encourage cessation of tobacco use to protect reproductive health(14). Moreover, smokeless tobacco has been known to lead to stromal inflammation and cellular edema, which can further exacerbate the damage to the uterus. This is consistent with this study, as results of the current study showed that the use of smokeless tobacco in rats led to impairment in the endometrial receptivity & angiogenesis.
It is significant to note that although current study was conducted in rats, the findings are likely to have implications for human health as well. Previous studies have shown that the effects of tobacco use on the reproductive system are similar in rats and humans. Therefore, it is essential to further investigate the potential impacts of smokeless tobacco use on reproductive health in human populations. The present study provides evidence that the use of smokeless tobacco can have significant impacts on the structure and function of the uterus, leading to myometrial degeneration, fibrosis, and edema. These findings underscore the need for increased public health efforts to educate women on the potential dangers of smokeless tobacco use and to motivate cessation of tobacco use to protect their reproductive health.

CONCLUSION

The study has shown substantial differences in the weight of the uterus and hormonal levels between different groups of rats based on the smokeless consumption. The use of smokeless tobacco was associated with reduction in the weight and hormonal levels in rats. Further research is needed to confirm and expand these findings in human subjects.

CONFLICT OF INTEREST:

Authors declare no conflict of interest

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ETHICAL APPROVAL:

This study was approved by Local Ethics Committee.

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Research Article

PREPARATION AND CHARACTERIZATION OF GLUTATHIONE LOADED POLYVINYL ALCOHOL ELECTROSPUN NANOFIBERS

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ABSTRACT
Reduced glutathione, or L-glutathione, is a tripeptide protein that occurs naturally in almost all cells of the human body. It is an antioxidant and plays a significant role in neutralizing oxidative stress. Oxidative stress is responsible for promoting many diseases and abnormalities in the body. This antioxidant decreases with time, and resulting in a number of disorders. To overcome these issues, experts recommend taking glutathione supplements. This study was aimed to design glutathione-loaded polyvinyl alcohol nanofibers, considering the properties of nanofibers that could be used as glutathione supplements to improve the deficiency of glutathione in the human body. With the electrospinning technique, poly (vinyl alcohol) loaded glutathione nanofibers were designed. The prepared nanofibers were characterized using Scanning Electron Microscopy (SEM), Fourier Transform Infrared Spectroscopy (FTIR), X-ray diffraction (XRD), and Ultraviolet-Visible Spectroscopy (UV–Vis) techniques. The antioxidant activity of the nanofibers was also determined; the activity indicated the eradication of free radicals.

Key Words: Glutathione loaded PVA, PVA electrospun nanofibers, Preparation and characterisation of Glutathione

INTRODUCTION

Human body is a combination of dynamic and complex systems, where every single cell is responsible for performing its work and playing its part in the system. All the systems result from the combination of these very tiny cells. Most of the normal and healthy cells in the body divide throughout our lives and replace themselves in a precise manner (1).

Humans are oxygen-consuming, so they are sometimes at risk of oxidative stress. Free radicals are exceedingly receptive synthetic compounds that can damage these cells. They are made with a loss or gain of an electron in a molecule. Free radicals are generally framed in the body and assume a critical role in many normal cellular processes; however, an increase in free radicals may harm every fundamental part of the cell. The harm to cells caused by free radicals, particularly the harm to DNA, may result in development and advancing diseases and other health conditions (1)

Free radicals are created as a by-product of metabolism. These free radicals wildly hunt for further molecules to stabilize in the body to latch onto; as a result, a single free radical produces another free radical. Consequently, a cascade of free radicals results in tissues injury(1). The body has several mechanisms to minimize radical-induced damage and repair damage, such as the enzymes superoxide dismutase, catalase, and glutathione peroxidase and glutathione reductase. Antioxidants are chemicals

that interact with and neutralize free radicals, thus preventing them from causing damage. They inhibit oxidation, therefore preventing the production of free radicals (2, 3). Reduced Glutathione (GSH) is a naturally occurring abundant tripeptide protein. This protein is a highly reactive compound. Glutathione plays dynamic roles within a cell. Glutathione follows a simple mechanism, i.e. it donates electrons to free radicals, or molecules with unpaired electrons, to neutralize them and preventing them from causing cellular damage (4, 5).

Reduced Glutathione

Reduced Glutathione or L-glutathione, a naturally occurring abundant tripeptide protein made up of 3 amino acids: Glutamic acid, Cysteine and Glycine, is found in almost all cells. This protein is a highly reactive compound. It mostly found conjugated to other molecules and compounds through its sulfhydryl moiety. Glutathione plays dynamic roles within a cell. Glutathione is a cellular detoxifier that maintains the redox state, antioxidation, immune response modulation, xenobiotic and drug detoxification, and protecting cells from damage by environmental toxins, free radicals, carcinogens, bad fats and peroxides are some essential roles played by glutathione (4, 5, 6).

Reduced glutathione donates electrons to free radicals, or molecules with unpaired electrons, to neutralize them and to prevent them from causing cellular damage. It is the essential detox and safeguarding operator responsible for restoring antioxidants (7, 8). Glutathione, *"The Detoxifier"*, helps break down the adverse effects of environmental toxins. The liver has a high concentration of glutathione. The liver executes hundreds of functions; one such function is detoxification (4, 5, 7). Throughout the body, various immune functions are supported by glutathione, *"the Booster"*. T-cells cannot function properly without glutathione, also vitamins C and E need glutathione to function appropriately (8, 9).

Oxidative stress and Free radicals

Available literature reported that glutathione deficiency adds to oxidative stress, which, impacts the advancement of a number of disorders, including Alzheimer's disease, Parkinson's disease, liver dysfunction, cystic fibrosis, sickle cell anaemia, malignant growth, coronary artery disease, stroke, and diabetes (10). Oxidative stress in the kidneys may cause kidney issues or even kidney failure, contingent upon its seriousness (11).

Different studies have reported that the body makes less glutathione as it ages. In women, glutathione concentration decreases at the start of menopause and continues to remain lower. Delayed oxidative stress from low glutathione levels in older individuals can make the bones weaker and may add to osteoporosis. Cells drained of glutathione are vulnerable to harm. Low levels trigger a course that at last prompts cell damage and death, which quickens the process of ageing (12, 13). Decreased action of glutathione peroxidase and low degrees of glutathione are associated with high oxidative stress and an increased probability of heart attack. Cardiovascular illness is, to a greater extent, initiated by oxidative stress in heart tissues (14-16).

Glutathione keeps the liver sound by neutralizing the oxidative stress that can prompt liver illness. It is significant in detoxing the liver and ensuring its sulphur-rich antioxidant pathways. When tackled with damaging ingredients, the liver will produce more glutathione to overcome the harm (17-19). Inadequate antioxidant agents, including glutathione, might exacerbate cell death in the liver. As a result, it can cause fatty liver disease in both the individuals who alcoholics and the non-alcoholic individuals. Glutathione has improved proteins, enzymes, and bilirubin levels in the blood of people

with alcoholic and non-alcoholic fatty liver disease (20). Several studies have recommended critical oxygen-free radicals (OFR) function in developing tumours and cancer (21).

Glutathione plays a fundamental role in almost every system of the human body. However, with the advancing age glutathione efficiency declines in human body due to many factors, such as eating unhealthy food and being exposed to a toxic environment for an extended period of time (1). To combat these issues, this study attempted to devise a way to design glutathione-carrying nanofibers. The distinctive properties of fibers have gotten extraordinary consideration from mainstream researchers as a reasonable contender for drug delivery applications. Nanofiber membranes from biopolymers can be used as a drug carrier. As a result, nanofibers provide significant bioavailability improvement (22,23).

The unique properties of fibers have received significant attention from the scientific community as suitable candidate for drug delivery applications. Their properties include high surface-to-volume ratio, high porosity, adjustable pore size and morphological similarity to the extracellular matrix (8-11). This study aimed to come up with a way to design glutathione-carrying nanofibers. Electrospinning is a technique used to design nanofibers. Electrospinning is a process in which a charged polymer jet is collected on a grounded collector.

MATERIALS AND METHODS

Materials

Reduced Glutathione: The drug L-Glutathione was purchased from bioWORLD Company, Dublin, USA.

Poly (vinyl alcohol): Poly (vinyl alcohol) (PVA) is a non-toxic, biodegradable, water-soluble synthetic polymer. It is used as an inactive ingredient that works as the medium for a drug or other active substance and as a surfactant for forming polymer-encapsulated nanofibers.

It is also considered a Generally Regarded As Safe (GRAS). Poly (vinyl Alcohol) was able to encapsulate glutathione. These were the reasons to use PVA as a polymer here (24), PVA was acquired from the lab.

Vitamin C: Vitamin C served the purpose of hindering the oxidation of glutathione due to environmental oxygen (25). CECON tablets (Vitamin C) were procured from Abott-Pharma (USA). Water served the role of solvent.

Methods

A method that has grown immensely popular for nanofiber production is electrospinning. Electrospinning is a process in which a charged polymer jet is collected on a grounded collector. Electrospinning involves using voltage to draw a jet of polymer solution from a syringe/ pipette source towards a collector. High voltage comes to aid in creating a repulsive force and charging the particles. Jet erupts from the tip of the syringe/ pipette as soon as the repulsive force overcomes the surface tension of the solution. High voltage also helps draw a fiber from the tip of the syringe/ pipette. As the charged jet accelerates towards regions of lower potential, i.e., the collector, the solvent evaporates while the entanglements of the polymer chains prevent the jet from breaking up. Collectors could either be rotating or stationary. Rapidly rotating collectors result in aligned nanofibers, while stationary collectors produce randomly oriented fiber mats. This results in fiber formation (26,27).

In its essential practice, this process consists of a pipette to hold the polymer solution, a collector and a voltage supply in the kV range. The jet is electrically charged, and the charge causes the fibers to bend so that every time the polymer fiber is twisted, its diameter is reduced. The fiber is collected as

a web of fibers on the surface of a grounded target. Multiple trials were taken to prepare nanofibers. Both rotating and stationary collectors were used separately.

A 3ml solution was prepared, and substances were added through calculations. The tube solution added 0.27g of PVA (9% of total weight) to the 2.7ml water. The solution was stirred on the electronic stirrer at 100 rpms. 0.015grm of CECON, 10% of the drug's weight, was added to prevent the drug from oxidizing. No temperature was provided once the PVA was dissolved, and CECON was kept on the stirrer to dissolve completely. For almost 20 minutes, the solution was further kept for stirring. When the solution was back at room temperature, the 0.15grm, 50% of PVA weight, of the glutathione was added and kept further for stirring.

Once the solution was prepared, the polymer solution was filled in the syringe, the plastic tip was connected to the syringe, the anode, a copper electrode, was inserted in the polymer solution-filled syringe, and the positive terminal of the power supply was connected to the electrode. The collector end was set to collect the fibers; butter paper and aluminum foil were used for collecting purposes, and the negative terminal from the power supply was connected to the collector plate. A black screen and light source were set to help focus or visualize the fibers. The syringe was firmly set on the handle stand. Once the setup was ready, the power supply was turned on at 12K volt.

The fabrication and synthesis of GSH-loaded PVA nanofibers were conducted at the Nanomaterials Research Group, Department of Textile Engineering, Mehran University of Engineering and Technology, Jamshoro, Pakistan.

Methods of characterization

The prepared fiber sheets underwent some methods and techniques for characterization and analysis. These methods of characterization were:

Scanning Electron Microscopy (SEM) provides information regarding the sample's composition and surface topography. The morphology of nanofibers was studied using a field emission scanning electron microscope (S-4800; Hitachi Ltd. Japan). SEM samples were coated with gold and examined at an accelerating voltage of 15 kV. The nanofiber diameter was calculated using ***ImageJ software***.

Fourier Transform Infrared Spectroscopy, or FTIR Analysis, is an analytical and diagnostic method used to recognize organic, polymeric, and, in some cases, inorganic materials. In this method, infrared light is used to perform scanning to perceive chemical properties. The chemical structure of nanofibers was analyzed using *FTIR spectroscopy* (Thermo Nicolet 5700, Thermo Fisher Scientific Inc. USA). For data analysis and curve fitting, Origin Pro 8 software was used.

X-ray diffraction is an X-ray-based technique where the material interacts with an x-ray beam of a specific wavelength. The beam gets dissipated, relying upon the crystal structure of the sample, and creates a plot with intensity elements as a function of 2 theta. The crystallinity of nanofibers was analysed using XRD, model D/max-IIB, and Rigaku RINT-2000 diffractometer with a source of filtered CuKα radiation. The measurement was performed at 40kV and 40mA with a diffraction angle of (2θ) between 5° and 70° at a scan rate of 4°/min. Origin Pro 8 software was used for data analysis and curve fitting.

Ultraviolet-Visible (UV–Vis) Spectroscopy was used to analyze the release behavior of GSH from GSH-loaded PVA nanofibers in PBS solution using a UV-1800-VIS Spectrophotometer (Shimadzu Corporation, Japan).

Antioxidant Activity was identified using the 2, 2-diphenyl-2-picrylhydrazyl hydrate(DPPH) assay. The DPPH stock solution in methanol was prepared. 1 mL of this stock solution was added to 3 mL of

GSH solution. After giving the combination a thorough shake, the mixture was let to stand at room temperature for 30 minutes. Afterwards, a UV-visible spectrophotometer was used to detect the absorbance at 517 nm (28). Antioxidant activity was estimated by calculating the percentage inhibition ratio by the following formula;

$$Inhibition\ ratio\ (\%) = (AC-AS)/AC \times 100$$

where AC was the absorbance of the control, and AS is the absorbance of the testing sample (GSH).

RESULTS

SEM Analysis: As stated earlier, SEM gives information related to surface topography. Figure 1 shows the SEM images of the designed GSH-loaded PVA nanofibers. With the aid of ImageJ software, the diameter of GSH-loaded PVA nanofibers was attained, and their average was found to be 57.99967 nm. In contrast, following the same method for neat PVA fiber sheets, the average diameter was calculated to be 25.5153 nm.

FTIR Analysis: FTIR gives information about chemical structure and behavior of a compound. The IR table is followed to understand the chemical bonding of the functional groups in the compound. This table tells the range of the energy at which different functional groups lie in IR spectra; this allows us to identify which group would change, i.e. absorbance of IR radiation at which wave—ultimately allowing us to understand the presence of functional groups and their behavior in the compound. The data obtained from the FTIR spectroscopy is plotted both on OriginPro.

As shown in Figure 2, the deep and broad trough between 3500 and 3000 cm-1 represents the presence of alcohol, OH group, a fundamental element of PVA. The narrow and sharp groove just on the right of 3000 cm-1 shows the presence of the CH bond; the CH bond is common in both GSH and PVA. Another deep, narrow trough on the left of 1500 cm-1 reflects the C=O, amide presence, a bond in GSH. This result was analyzed by using IR tables.

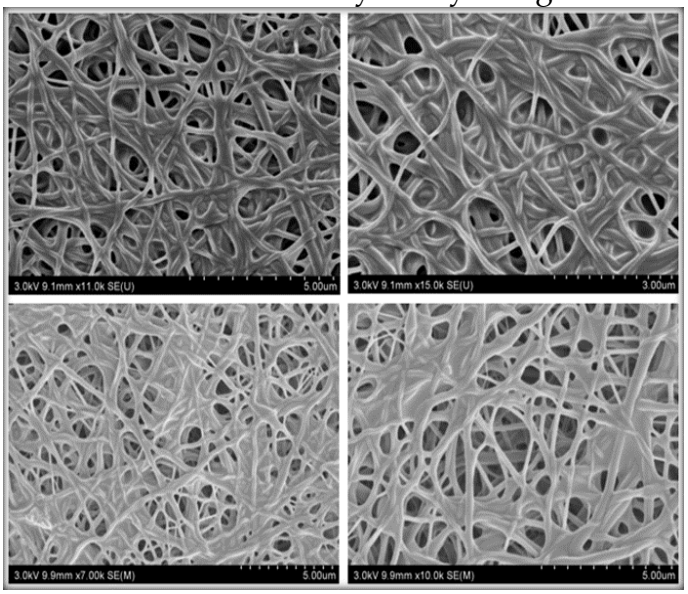


Figure 1. SEM Images of GSH-loaded PVA nanofiber

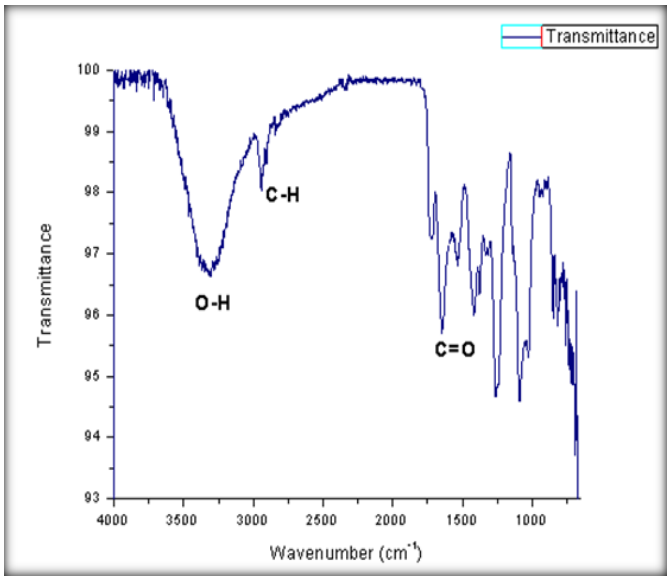


Figure 2. Data obtained from FTIR analysis plotted on OriginPro

XRD Analysis: XRD gives an understanding of whether the compound is crystalline or amorphous at the level of the unit cell. Figure 3 shows the XRD result and pattern of GSH-loaded PVA fibers, intensity vs. angle. The data obtained from the crystallography is plotted both on OriginPro. As shown in Figure 4, at

X=10.08° there is a rise in the pattern of GSH-loaded PVA nanofibers; when 2θ varies from 18° to 26°, there is a rise in the XRD pattern. The pattern shows the dominance of the PVA, but at X=22.56°, the intensity is 1239, which is 93% (1324 is the 100% intensity).

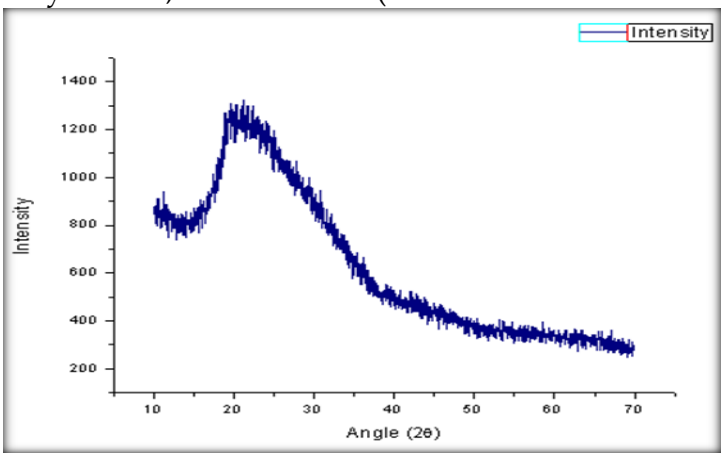
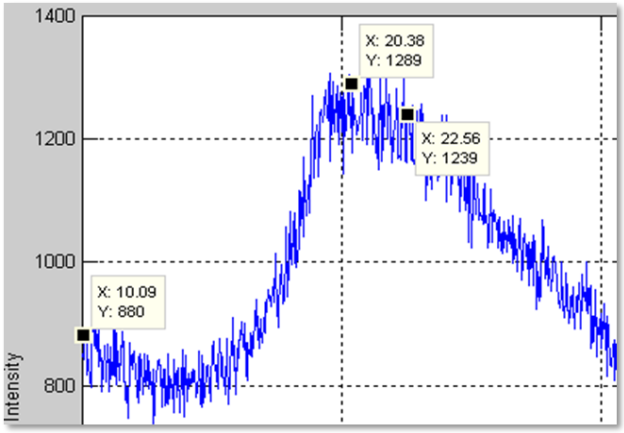


Figure 3. Data received from XRD analysis plotted on OriginPro.



gure 4. XRD pattern of GSH-loaded PVA nofiber

UV-Vis Analysis: Figure 5 shows the UV/Vis result and pattern of GSH-loaded PVA fibers, absorption vs. wavelength. Phosphate Buffered Saline (PBS), a universally accepted salt solution used in biological research, was prepared by dissolving 8 g of NaCl, 0.2 g of KCl, 1.44 g ofNa2HPO4, 0.24 g of KH2PO4 in 1-liter distilled H2O (Average pH 7.2 ~7.4). The GSH exhibited a maximum at 206 nm. For this purpose, a 10mg sheet of GSH-loaded PVA fibers is added to the 30ml Buffer solution. The absorbance values were obtained from the prepared solution with the help of a UV-Vis Spectrophotometer. The absorbance value(s) of the solution is observed for 10 minutes, with an interval of 5 minutes. The data obtained from the spectroscopy is plotted on OriginPro. Antioxidant activity is presented in Figure 6 and Table 1.

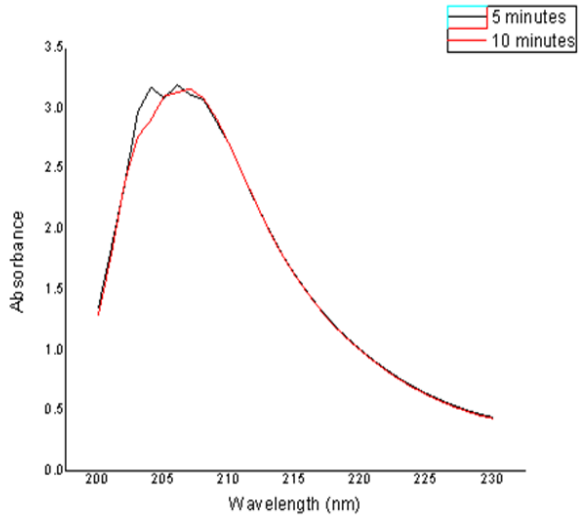


Figure 5. UV/Vis result and pattern of GSH-loaded PVA fibers

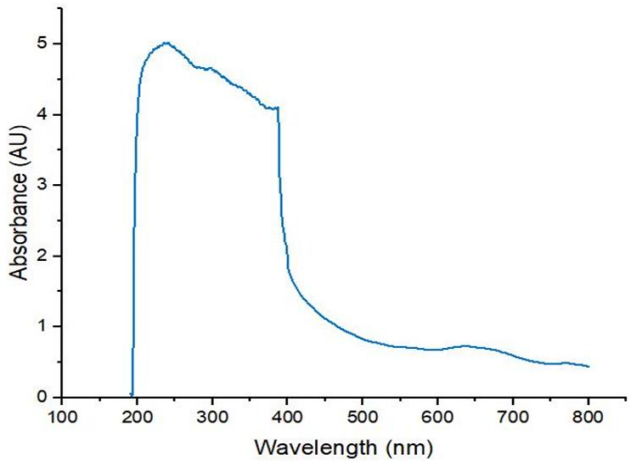


Figure 6. Antioxidant activity of GSH

Table 1. Radical inhibition ability of GSH

Sample type	Absorbance at 517 nm	% of radical inhibition
Control	1.092	-
GSH	0.7807	28.5%

DISCUSSION

Polyvinyl alcohol is a non-toxic and biocompatible polymer that degrades in the body; therefore, it is regarded as a safe material for research purposes. Due to its properties to form chains, it has been generally used as a nano-carrier for many applications. Because of these abilities, polyvinyl alcohol is used as a carrier for glutathione (29,30)

Glutathione is the most dominant antioxidant. It is continually at work in every single cell of the body. Nevertheless, the degree of glutathione in the body diminishes as part of the natural ageing process. Levels are affected adversely when the body is under stress from ailment; prolonged exposure to toxic substances additionally decreases glutathione advantages to the body. Boosting the body's capacity to yield glutathione with nanofibers will give numerous medical advantages, including decreased oxidative stress (31, 32).

Different drugs of abuse (for example, cocaine and alcohol) increment the generation of responsive oxygen species. These, thus, can modify the brain and cause harm. A few studies propose that expanding glutathione can help defeat addictive practices, which span from eating disorders to alcohol/drug abuse. Expanding antioxidant defense not only ensures the brain but also helps detox destructive substances from the body. Chronic alcohol abuse decreases glutathione in the liver. Rising glutathione levels improved liver capacity during restraint. Liquor misuse likewise expands oxidative stress in the lungs, which can frequently promote diseases, for example, pneumonia. Glutathione might protect the lungs by lessening oxidative stress (33, 34)

In an investigation of 20 individuals with a chronic kidney infection on hemodialysis, glutathione improved kidney work (16). As suggested by Huang et al., renewing glutathione levels may slow the maturing procedure, toughen the bones, and counteract age-related decay (20). Studies have also shown that glutathione can lessen free radicals and, thus, may avert stroke or heart attack (23). Glutathione was most effective when given to individuals with fatty liver disease intravenously (30).

The lower degree of glutathione can build inflammation in the airways and cause asthma. In mice with asthma, expanding glutathione with NAC brought down inflammation and amended the manifestations. Chronic Obstructive Pulmonary Disease (COPD) is a lung illness brought about by long-term oxidative harm. Growing glutathione reduces free-radical lung harm, diminishing the probability of evolving COPD (35, 36)

In numerous chronic diseases, weak immunity and an amplified degree of infections are connected to low glutathione levels. The chronic inflammation brought about via autoimmune sicknesses can build oxidative stress. These maladies incorporate rheumatoid arthritis, celiac disease, and lupus. As per studies, glutathione lessens oxidative stress by decreasing the body's immunological reaction. Autoimmune diseases assault the mitochondria in cells. Glutathione attempts to ensure mitochondria’s safety by dispensing free radicals (37, 38).

Individuals with sleep apnea have significant levels of oxidative stress and, thus, exhausted glutathione levels. In one examination, increasing the levels improved their resting quality. The leading causes of complete loss of sight are glaucoma and cataracts. As oxidative stress is responsible for both, improving glutathione levels may help protect the eyes (39, 40).

Oxidative stress brings down glutathione in individuals with skin acne. Expanding glutathione levels may clean a person's acne by neutralizing oxidative stress and encouraging skin recovery. Glutathione lightens the skin in healthy women. It decreases the movement of skin cells that make dark pigments

(melanin). Glutathione may help even out the presence of dark skin patches that show up with maturing. Various personal-care items containing glutathione are promoted for their alleged skin-brightening impacts. These items incorporate cleansers and creams. In any case, a few people take glutathione supplements for skin-brightening (15, 41-42).

In different studies, glutathione has been found to attack cancer cells and even reduce the contrary effects of other cancer treatments. A study showed the effects of glutathione in ovarian cancer cells. According to the published study, it was observed that IV glutathione triggered the death of cancer cells. The study results show that extracellular glutathione caused cancer cells' apoptosis (cell death) by triggering DNA damage in cancer cells (4). Studies are going on to highlight different roles played by glutathione that finally control tumour evolution and improve the use of glutathione-based drugs to specifically target this detoxifying system in cancer treatment to increase therapeutic response (43).

CONCLUSION

Glutathione plays a vital and dynamic role in almost all the functions of the human body. Nevertheless, with age and an unhealthy diet, the levels of glutathione decrease with time. In such cases, glutathione supplements are recommended. This study synthesised the PVA nanofibers loaded with GSH due to the myriad benefits of the nanofibers over conventional medicines. Further studies are required to explore clinical benefits of GSH nanofibers.

CONFLICT OF INTEREST:

Authors declare no conflict of interest

FUNDING SOURCE:

The study did not receive any external funding

ETHICAL APPROVAL:

The study was approved by local Research Ethics Committee.

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Research Article

EVALUATION OF DIFFICULTIES AND REPRODUCTIVE HEALTH ISSUES FACED BY FLOOD-AFFECTED PREGNANT WOMEN IN REFUGEE CAMPS

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ABSTRACT

Natural disasters jeopardize routine life, including health care system. This cross-sectional study was conducted to determine the difficulties faced by flood-affected pregnant women in refugee camps of the Hyderabad region of Pakistan. This study was conducted from October 2022 to September 2023. A field survey was done as part of quantitative research to find women affected by catastrophe who were residing in shelter camps. The primary data collection took place close to Jamshoro, Kotri and Hyderabad City in the regions where temporary flood-relief shelters were constructed and flood affected pregnant ladies referred to tertiary care (Countess Lady Duffirin Fund) Hospital with reproductive health issues e.g. high risk pregnancies for antenatal care, correction of anemia, control of blood pressure and diabetes, normal vaginal deliveries and emergency or elective caesarean sections. Eight hundred thirty-two patients were recruited, including 69.2% aged 15 – 25 years old, 44.2% with 2nd trimester of gestational age. All patients complained about unavailability of transportation, complained about the provision of medicine (62%), antenatal care (3.8%) disposable waste (3.8%), clean water supply (3.8%) and provision of food (19.2%). Women in relief camps face multifactorial problems which adversely affect their health including reproductive health.

Key Words: Flood, pregnant women, Sindh, Pakistan, refugee camps.

INTRODUCTION

Natural disasters occur in almost all regions of the world; some are more prone to earthquakes while others face floods more often. Recently, Sindh province of Pakistan was badly hit by floods jeopardizing life in Pakistan in particular Sindh. At least 650,000 pregnant women and girls were among the millions of people who have been seriously affected; 73,000 of them were anticipated to give birth within month's time after floods (1). Many of these mothers, according to the United Nations Population Fund (UNFPA), do not have access to the healthcare resources and assistance they require to deliver their children safely (2). Pakistani women were at high risk of maternal death in South Asia, which was feared to get even worst (3). Furthermore, pregnant women were among the population most severely impacted by the negative effects of climate change (4). Floods had badly destroyed healthcare system, in the province of Sindh, more than 1,000 healthcare facilities either completely or partially damaged (5).

In Baluchistan province, additional 198 medical facilities were destroyed. The massive damage done to the roadways and communication systems made it difficult to access healthcare facilities in less flood

affected areas. These obstacles affect pregnant women, young girls, and those looking to receive reproductive health services such as contraception.

The necessities of their families and child care were burden for women in this area of floods. In refugee camps, women discontinued breastfeeding because there was lack of energy and privacy. According to studies, 75% of displaced people experienced these problems as a result of stress, a lack of privacy, and unsanitary environments (6). Tent camps for displaced people provide a shelter, but are not secure settings for expectant mothers to give birth or even to stay for an extended period of time. A large proportion of these women were underage, pregnant, or living with female relatives like sisters, mothers, in-laws, or grandmothers (7).

The temporary shelters are made to provide a roof without taking health of women and girls into account. The pregnant women's needs were also altogether ignored. Which had a disproportionately negative impact on women and girls health. Women's health and safety in Pakistan had always been a serious concern; the humanitarian crisis had further increased their risk (8).

There is limited data available to explore health issues faced by pregnant women living in temporary camps after natural disasters in developing countries. Therefore, this study was designed to explore the difficulties faced by flood-affected pregnant women in refugee camps of the Hyderabad region of Pakistan.

METHODS

This study was exploratory in nature, used both quantitative and qualitative research methodologies conducted from October 2022 to September 2023. A field survey was done as part of quantitative research to find women affected by floods, and were residing in temporary shelter camps. These women were asked open ended questions, a qualitative interview method was adopted to get women's responses in their own narratives. The primary data collection took place close to Jamshoro, Kotri and Hyderabad City in the region where temporary flood-relief shelters were constructed and flood affected pregnant ladies referred to tertiary care (Countess Lady Dufferin Fund) Hospital with reproductive health issues including high risk pregnancies for antenatal care, correction of anemia, control of blood pressure and diabetes, normal vaginal delivery and emergency or elective caesarean sections. Social problems and difficulties in availing health care facilities faced by pregnant women, maternal health issues and data about fetal outcome were collected.

Each participant was personally interviewed by the researchers. Participants' consent was secured in order to utilize the data for scholarly publications. In order to get more insights about the problems, interviews were initially conducted in local language (i.e. Sindhi) and later translated into English. The research questions were addressed by carefully identifying themes from the data analysis.

Before beginning the formal interviews, all women were assured of their confidentiality and the rationale and the purpose of the study was also explained. All women were then signed informed consent for the use of data and volunteer involvement in research. Every attempt was made to give women a trustworthy environment. Due to the delicate nature of the research issue, interviews were done one-on-one.

Statistical analysis

Data were stored and analyzed using IBM-SPSS version 23.0. Number and percentages were reported on baseline characteristics of the study population. A Bar diagram was used to report the problems faced by pregnant women. Descriptive on access to the health care center and availability of screening tests were also reported for study population.

RESULTS

A total of 832 women were included in this study, out of which 69.2% were aged between 15 and 25 years old and 44.2% were presented in 2nd trimester in gestational age. Half of the participants were from low socio-economic class (50%) and 32.7% had only completed their primary education, 44.2% were booked, 40.4% had more than 20-days duration of stay in the camp. A summary of the data is given in Table 1. Half of the women recruited in this study had active health complaints in need of medical care. Figure 1. Presented the problems faced by pregnant women. All women complaint about unavailability of transportation. There were also complaints about antenatal care, disposing off waste, clean water supply and provision of proper food. A total of 53.8% denied access to healthcare centers, 32.7% agreed on the availability of the screening test for communicable diseases, and none was reported for the availability of screening tests for non-communicable diseases. A summary is presented in Table 2. Most common problem was anemia, followed by malaria and hypertension. A list of health related issues is presented in Table 3. Early preterm labor and miscarriages were observed. A summary of outcome is given in Table 4.

Table 1. Demographic characteristics of pregnant women living in temporary camps made for flood affected population of Sindh (n=832)

Characteristics		*n*	*%*
Age Group	15-25 Years	376	69.2
	26-35 years	140	28.8
	36-45 years	16	1.9
Gestational age in trimesters	1st trimesters	352	42.3
	2nd trimesters	368	44.2
	3rd trimesters	112	13.5
	4th trimesters	0	0.0
Maternal Education	Nil	452	54.3
	Primary	272	32.7
	Middle	108	13.0
Socio Economic status	Low	216	50.0
	Middle	368	44.2
	High	48	5.8
Booking status	Booked	368	44.2
	Un-booked	462	55.8
Duration of stay	10-days	256	30.8
	11-20 days	140	28.8
	More than 20 days	336	40.4
Delivered	Miscarriage	42	5.0
	Preterm labor	37	4.4
	Vaginal delivery	109	13.1
	LSCS	85	10.2
Un delivered	Ante natal check up	559	67.1

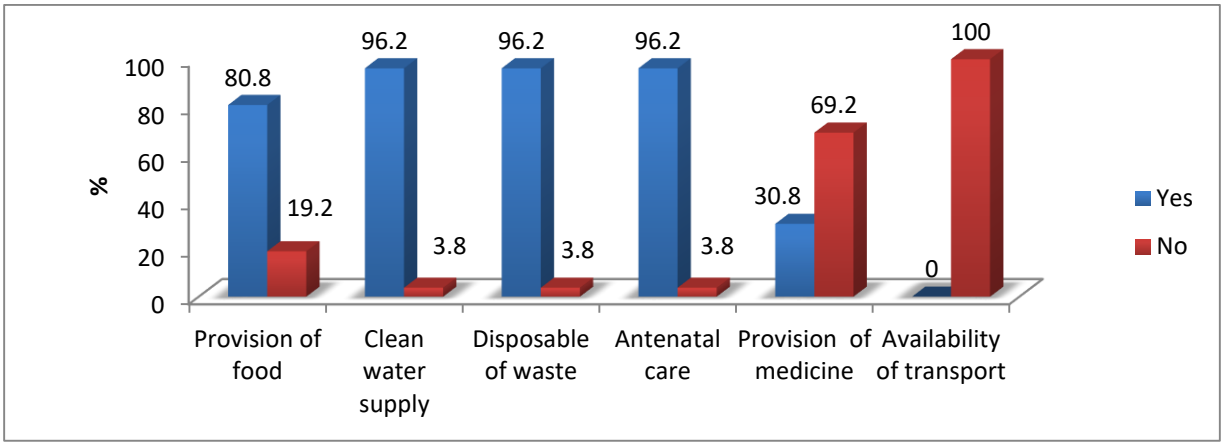

Figure 1. Summary of the problems reported by the women living in temporary camps for flood affected population in Pakistan

Table 2. Outcomes of access to the health care center and availability of screening tests

Questions		**n**	**%**
Access to the health care centre	Yes	112	53.8
	No	96	46.2
Availability of screening tests for communicable disease	Yes	68	32.7
	No	140	67.3
Availability of screening tests for Non-communicable disease	Yes	0	0.0
	No	208	100.0

Table 3. A summary of the active complaints in pregnant women living in temporary camps in flood affected population in Sindh

Complaint	**n**	**%**
Anemia	556	66.8
Miscarriage	42	5.0
Malaria	177	21.2
Dengue	76	9.1
Hypertension	87	10.4
Pre-eclampsia/ eclampsia	38	4.5
Preterm labour	37	4.4
Antepartum hemorrhage	51	6.1
Postpartum hemorrhage	62	7.4

Table 4. Fetal outcome of the pregnancies in women living in flood affected areas of Sindh

Outcome	**n**	**%**
Miscarriage	42	5.0
Preterm delivery	37	4.4
Still born	17	2.0
Early neonatal death	49	5.8
Remained alive	128	15.3

DISCUSSION

This study presented health issued faced by pregnant women living in temporary flood relief camps. Majority of women were young and in 2nd trimester of pregnancy. They faced many health related issues and there was a considerable number of early neonatal deaths. In the same environment as a natural disaster, women are more vulnerable than males. Women have a high mortality risk due to pre-existing gender inequity, sociocultural community factors, and poverty. Due to their lack of access to prenatal and obstetric care during any disaster or humanitarian emergency context, pregnant women are especially susceptible.

In this study availability of transport and medicine was satisfactory as responded by majority of pregnant women in the refugee camps of the Hyderabad region of Pakistan. Hundred percent of the pregnant women responded that there is no availability of screening tests for non-communicable diseases, while most of the pregnant women complained of the non-availability of screening tests for communicable diseases and lack of access to health care centers. Humaira Maheen et al conducted a study in 2011 on women's experiences of pregnancy and giving birth in natural disaster settings in Pakistan. In the relief camps, there were no skilled birth attendants, ambulances, breastfeeding stations, or postpartum care for women. When giving birth in unsanitary conditions in the camps, women sought the help of the customary birth attendants (9).

In the present study, there were 832 samples, 69.2% were aged 15 – 25 years old, 44.2% with 2nd trimester of gestational age, 32.7% were up to primary education, 50% were from low socio-economic class, 44.2% were booked, 40.4% had more than 20-days duration of stay. In the current study pregnant ladies were referred to CDF Tertiary care hospital with various maternal obstetrical complications and for delivery or termination of pregnancy, of which 273 women delivered, and the most common health issue was anemia in pregnancy followed by Malaria, hypertension and dengue fever in pregnancy respectively, regarding fetal outcome miscarriage found in 42(5%) patients, preterm delivery 37 (4.4%),stillborn 17(2%) ,early neonatal death 49 (5.8%), while 128(15,3%) babies remained alive and healthy. Another study was conducted by Shahla Baloch et al. on screening of reproductive health problems in flood-affected pregnant women in district Jamshoro. A total of 571 women overall (15.01%) experienced various obstetrical issues over the research period (2011). The majority of these women(n= 313, 54.81%), were between the ages of 21 and 30, and 359 (62.87%) were in the last stages of pregnancy. Anemia was the most prevalent obstetrical issue among flood-affected women, occurring in 399 (69.87%) instances (10). According to Memon, F. S. et al, a total of 20 women were interviewed in the flood-prone areas of Sindh. According to study a majority of women encountered various forms of physical and mental violence from partners and even total strangers. When women were displaced and stayed in temporary housing during a post-disaster period, the rate of such violence was increased further (11).

In the current study, the majority of women complained of a lack of provision of food, clean water supply, disposable of waste and antenatal care. A study by AbulKalam Azad examines flood-induced vulnerabilities among women in northern Bangladesh. Women were unable to carry out their normal responsibilities at home due to challenges in finding appropriate housing, food, safe water, and fuel for cooking, as well as issues with maintaining personal hygiene and sanitary conditions. These are all issues that pertain to women's gender identities and societal responsibilities (12). In another study from Bangladesh, due to maternal problems, a lack of prenatal care, and a shortage of doctors during

flooding, pregnant women experience severe suffering. Finding a qualified attendant at the moment of delivery is challenging, and the patient with birth problems is referred to the healthcare facility. The sole means of transportation are boats. When women are being transported from their communities to hospitals by boat, the majority of maternal deaths take place during that transportation (13). Mehwish Muhammad Ali et al concluded that there was a shortage of food and potable water in flood affected areas. Additionally, there was no food available for women (14).

According to Nafeesa Naveed et al, tent residents reported sharing a room with more than four people. 31 people were using tents; 11 shared a room with 4-6 people, 19 shared a room with 7–10 people, and 1 was living with more than 10 people in a room. Regarding food, 15 participants (21.1%), as opposed to 56 (78.9%), stated that they received a full meal twice a day. They all claimed to have ingested carbohydrates in some way, along with some proteins and fruits, but no nuts were consumed (15).

The study was conducted on a large sample of pregnant women living in flood affected camps and a comprehensive interviews were conducted. It is considered as strength of the study. However, no interventional strategies were adopted is a limitation of this study.

CONCLUSION

Women living in flood relief camps face multiple health related issues, which become more serious when comes to pregnant women. Anaemia was the most common condition seen in pregnant women. There were also a considerable number of early neonatal deaths. Thus there is need to establish interventional strategies to reduce maternal health issues and neonatal deaths.

CONFLICT OF INTEREST:

Authors declare no conflict of interest

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The study was approved by local ethics committee.

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Research Article

EVALUATION OF THE PATTERN OF NECK PAIN WITH FORWARD HEAD POSTURE (FHP) AMONG SEWING MACHINE OPERATORS- A CROSS-SECTIONAL STUDY

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ABSTRACT

One of the very common negative effects experienced by operators and workers of sewing machines is neck pain. The use of sewing machines in a forward-leaning position over an extended period of time contributes to neck strain and promotes bad postures like the Forward Head Posture (FHP). The objective of this study was to determine the prevalence of FHP and neck pain among sewing machine operators in tailors and garment factories of District Swabi, Pakistan. This cross-sectional study was carried out on a total of 223 users of sewing machines while seated (97 women and 126 men). The study was conducted in Swabi District from October 2022 to February 2023. The outcomes were evaluated using a numerical pain rating scale and the Neck Disability Index (NDI). According to the Numerical pain Rating Scale (NPRS) for neck pain, 24 participants (10.8%) reported mild discomfort, 79 participants (35.4%) reported moderate pain, and 120 participants (53.8%) reported severe pain. Only 13.9% (n=31) of the participants (n=192) had a normal head position. The majority of the participants were hunched forward. The NPRS had a mean of 3.43 (± SD 0.49), the NDI mean was 3.43 (± 0.68), and the cranial vertebral angle (CVA) mean was 1.13 (±SD 0.34). According to the findings of the current study, FHP and neck pain are quite common among individuals who use sewing machines, and a large percentage of these people also have FHP and neck discomfort.

Key Words:. : Neck pain, Forward Head Posture, Sewing Machine related neck problems

INTRODUCTION

Neck pain is one of the common public health issues and most prevalent musculoskeletal condition (1, 2). It ranges in severity from mild discomfort to excruciating pain that is incapacitating (3). While mechanical and degenerative reasons are more likely to cause chronic neck pain, poor posture, neck strain, sports and work-related accidents, and mental health issues including anxiety and depression are the causes of less severe neck pain (4). In the sagittal plane, forward head position (FHP), is the most prevalent postural abnormality (5). Any alignment in which the external auditory meatus passes through the shoulder joint ahead of the plumb line is considered it. Although there are a number of ways to calculate FHP, numerous studies have found that the reliable indicator for doing so is the cranial vertebral angle (CVA) (6). Numerous assessment techniques, including observation, instrumental (electronic head position instrument, cervical motion instrument), imaging, conventional radiography, and photography, have been used to evaluate the position over the years (7). It has been demonstrated that photogrammetry is a sensitive, dependable tool for evaluating FHP that has good

radiography correlation. The angle of a horizontal line passing through Cervical vertebrae 7 (C7) and the imaginary line extending between C7 and the tragus are used to calculate CVA (6). This non-invasive method entails acquiring pictures, which are subsequently digitized using computer software for additional examination (8). The raised cervical lordosis curve's apex is located far from the centre of gravity in FHP. The head also advances forward. Nerve root compression is caused by FHP, which progressively shortens the posterior joint capsule, narrows the intervertebral gaps, and causes inappropriate compression at the zygapophyseal joint and posterior vertebral discs. Furthermore, these postural modifications result in functional alterations in the temporomandibular joint. FHP can result in decreased cervical range of motion, muscle ischemia, soreness, tiredness, inflammation, and protrusion of the nucleus pulposus, which can rotate the mandible and compress and irritate the retrodisc pad (9). Sewing machine operation involves a forward-leaning sitting position that is static and unnatural in terms of the angle of the knee and ankle, which continuously strains the neck muscles (10). Previous research has shown the common occurrence of neck pain among global garment workers (11). Sewing machine workers frequently experience work-related musculoskeletal disorders as a result of their extended working hours, insufficient breaks, and poor ergonomics, which increase their risk of neck, back, and shoulder injuries (12). Literature, however, indicates that there are few studies on the pattern of FHP and its connection with high-risk employment. Majority of the studies reported so far have focused on the relationship between neck pain and work postures rather than a normal body. This study sought to ascertain the association between neck discomfort and the cranio-vertebral angle in sewing machines at two clothing companies in Pakistan's Swabi District, as well as the rate of occurrence of FHP among these workers.

METHODS

A total of 223 sewing machine operators who worked in the sitting posture participated in this cross-sectional study, including 97 females and 126 males. Users of sewing machines who spent at least five hours a day in a seated position and those with more than a year of experience using sewing machines met the inclusion criteria. Individuals who were diagnosed with conditions that could impair cervical spine mobility, such as rheumatoid arthritis, traumatic neck injuries, idiopathic scoliosis, cervical spondylosis, bone cancer, and congenital neck problems or radiation, were excluded from the study. The study was conducted from October 2022 to February 2023, the study was carried out in District Swabi. Numeric pain rating scale (NPRS) and Neck disability index (NDI) were used for outcome measurement.

Neck pain assessment

The interviewer's questionnaire, which asked about personal information, employment history, knowledge of postural correction exercises, and the presence or absence of neck discomfort, was used to gauge the degree of neck pain. Using the NPRS, the level of neck discomfort was evaluated. It was thought improbable that the CVA measurement would have an impact on the severity of pain complaints. The participants were informed that neck pain was specifically defined as pain in the neck and/or upper trapezius area that they experience during work hours or at the conclusion of a shift due to their prolonged periods of standing in one position (13).

Measurement of cranio-vertebral angle (CVA), cervical flexion and extension

Two body spots were designated before CVA measurements were taken with photos. They were the tragus and the synovium of the seventh cervical vertebra. To make two points visible in the pictures, markers made of Styrofoam balls and 0.5 cm x 0.5 cm double-sided tape were used to mark them. In

order to reference the horizontal and vertical axes of the photographs, the participant was instructed to stand in front of a calibration table that had been adjusted to match their location. The calibration plate displayed the participant's registration number for identifying purposes. To ensure that every subject stood in the same spot, a footprint was placed on the ground. The placements of the tripod and camera were fixed to ensure uniformity throughout the data collection procedure. Measuring tapes were used to mark the subject's location in front of the board and the distance between the subject and the tripod in order to prevent any changes from altering the measurement. 100 cm from the lateral edge of the footprint, the camera was positioned on a tripod. The camera's height was changed so that the participant's tragus was in focus (7). The centre mark and the horizontal indicator bubble were overlapped by adjusting the camera mount (14). The subject was instructed to wait for an object on the wall while standing on a footprint in order to record the CVA. Subsequently, he was instructed to stand up with his weight evenly spread between his legs and arms. In order to make sure that the head and neck were in a relaxed, neutral position, the participant was asked to tilt their head forward and backward three times. To lessen distortion from stress, three pictures were obtained at two-minute interval (15).

Analysis of cranio-vertebral angle (CVA)

Every picture was evaluated on Kinovea software (0.9.4). The angle created between the line connecting the tragus-articular tendon of the seventh cervical vertebra and the horizontal line that passes through the spiral of the vertebra was used to calculate the CVA (Figure 1).

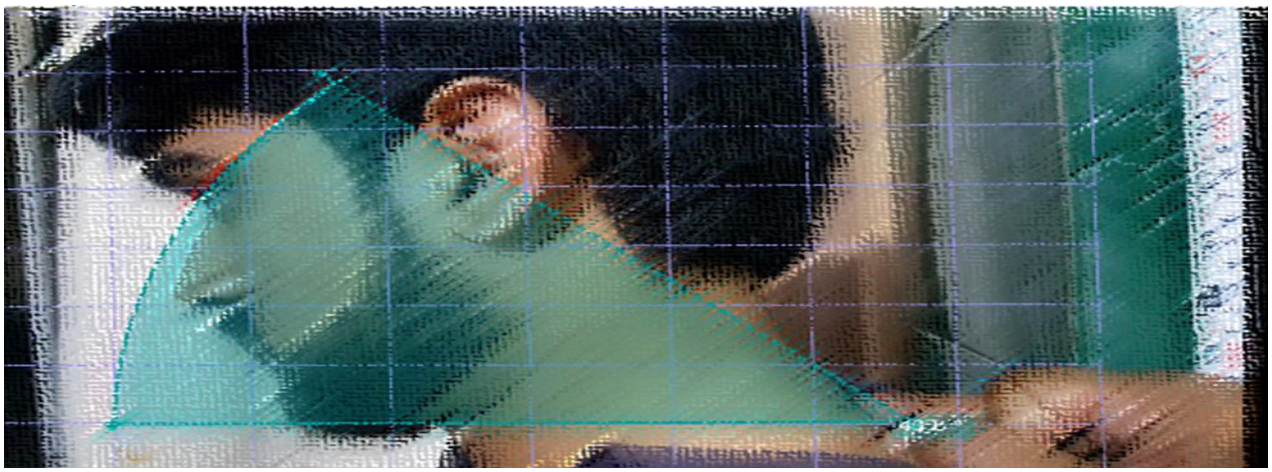

Figure 1: Method of analysis of cranio-vertebral angle

Statistical analysis

Data was analyzed by using Statistical Package for Social Sciences (SPSS 23.0). Data was presented in frequency distribution and percentages.

RESULTS

Out of total 223 participants; 126 (56.5%) were males and 97 (43.5%) were females. Out of these 121 (54.3%) were between the age group 25 to 35 years, 64 (28.7%) were 36 to 46 years and 38 (17%) were over 46 years. With respect to the duration of work 23.3% (n=52) were working around 4 hours/day and 76.7% (n=171) were working more than 4 hours/day. Which clearly showed that most of participants were working more than 4 hours/day. Regarding neck pain with respect to NPRS scale;

24 (10.8%) were in mild pain, 79 (35.4%) were in moderate pain and 120 (53.8%)were in severe pain. On NDI scale 5.8% were mildly disabled, 15.7% were moderately disabled and 78.5% were severely disabled. 171 participants were working more than 4 hours per day and 52 were working around 4 hours per day. 129 (57.8%) participants were dress tailors and 94 (42.2%) were factory workers. 86.1% (n=192) participants had FHP and only 13.9% (n=31) were reported to be normal. Which clearly showed that most of the participants were in FHP (Table 1). The mean NPRS was 3.43 (SD± 0.49), NDI was 3.43 (SD±0.68) and the mean CVA was 1.13 (SD±0.34). The association of the working hours and CVA showed significant results with (p-value < 0.001).

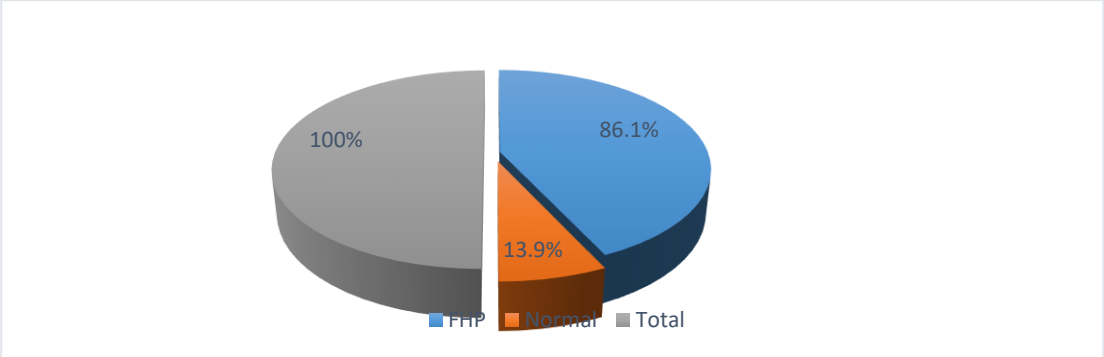

Figure 2: Showing the Frequency of Cervical vertebral angle.

Table 1: Showing the statistical Description of the study.

		Frequency	Percent
Gender (n=223)	Male	126	56.5%
	Female	97	43.5%
NPRS (n=223)	Mild pain	24	10.8%
	Moderate pain	79	35.4%
	Sever pain	120	53.8%
NDI (n=223)	Mild Disable	13	5.8%
	Moderate Disable	35	15.7%
	Sever Disable	175	78.5%
CVA (n=223)	FHP	192	86.1%
	Normal	31	13.9%
Duration of work (n=223)	Less than 4 hours	52	23.3%
	More than 4 hours	171	76.7%

DISCUSSION

The purpose of this study was to determine the pattern of FHP and the connection between neck discomfort and CVA in sewing machine workers. The photogrammetry approach, which has never used before in Pakistan's physiotherapy area, was employed in this study to quantify CVA.

Sewing machine operators exhibited FHP with 103 (64.67%) of them meeting the recommended standard of a CVA of 50˚or above. Numerous articles support the high prevalence of FHP among various occupations with similar postures, such as office workers, dentists, and call centre operators (15, 16). Sixty-eight of the 167 sewing machine users in the sample reported having neck pain at the end of their shift or during working hours. The prevalence of neck pain among seamstresses and clothing industry workers is in line with earlier studies' findings (16). Sixty-three (6.67%) of the sewing machine users displayed a forward head position, even though a CVA of 50˚or higher was thought to be the proper head position. Numerous studies have reported the high incidence of FHP in a range of positions with comparable postures, including call centre operators, dentists, display terminal employees, and office workers (17).

Of those who used sewing machines and reported having neck pain at work, 86.1% of participants had FHP. The high frequency of FHP among individuals experiencing neck pain is in line with earlier research by Ruivo, Pezarat-Corriea, and Carita (2019)(18) and Chiu et al. (2002) (19), which revealed 60.5% of FHP among academic staff experiencing neck pain. Among sewing machine users with neck pain, there was a negative connection observed between the severity of neck pain and CVA.

These results are in line with earlier research conducted between various professional groups by Subbarayalu and Ameer (2017) and Abbhas et al. (2016) (20). Similar results were seen in other studies including patients with neck pain by Contractor, Shah, and Shah (2018), Yip, Chiu, and Poon (2008), and Lau, Chiu, and Lam (2010) (21). These investigations also revealed a low-negative connection between the intensity of neck pain and CVA. Our theory that FHP correction may improve outcomes for individuals with neck pain is supported by the negative connection found between CVA and neck pain intensity, which shows that lower CVA values correspond to more severe neck pain. Our results showed that the link between CVA and the level of neck pain was, at most, modest, indicating that it might be one of the causes related to neck pain and that other aspects needs to be focused in further research. We were unable to establish a causal association between head posture and neck discomfort because this was a cross-sectional study, and self-reporting of the inclusion and exclusion criteria might have some recall bias, therefore it is taken as limitations of the study. Psychological stress, balance issues, or visual abnormalities that could influence head posture were not ruled out. Additionally, we did not examine the properties of the entire spine. Future research should take this into account since modifications to the lumbar and thoracic spine may have an impact on head posture.

CONCLUSION

The findings of the present study demonstrated that a significant number of sewing machine users who also had neck pain and a high prevalence of both conditions. The study found a small but statistically significant negative connection between neck discomfort intensity and CVA. Further studies are required to confirm findings of our study. Interventional studies to improve posture during working hours are needed to be done and make recommendations.

CONFLICT OF INTEREST:

Authors declare no conflict of interest

FUNDING SOURCE:
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ETHICAL APPROVAL:
The study was approved by local Research Ethics Committee.

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Research Article

EVALUATION OF LONG TERM SEQUELAE OF COVID-19 AMONG SURVIVORS AND THEIR PERCEPTION ABOUT THE DISEASE

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ABSTRACT

The study was conducted to evaluate the emotional, cognitive and behavioral effects among COVID 19 survivors. The data was collected from April 2020 to June 2021. Simple face to face and online data collection methods were employed, a questionnaire using likart type questions was used. For data collection, five point Likert scale questionnaire was designed according to the objectives of the study. The questionnaire included questions related to cognitive, emotional and behavioral aspects of the COVID-19 survivors. Additionally, it also explored the perceptions of the participants about the disease. A total of 90 participants were recruited in this study. All these had confirmed diagnosis of COVID 19 on Polymerase Chain Reaction (PCR) positive on nasal swab. The findings of this study indicate that most of the covid-19 survivors feel weakness, and depression after recovering from this viral disease. A considerable number of COVID 19 survivors experienced loss taste and smell for a prolonged period. According to their perception social gatherings were responsible for spread of the disease thus they strongly agreed upon lockdown strategy adopted in many countries.

Key Words: Post-COVID cognitive disorder, emotional disorder in COVID survivors

INTRODUCTION

Coronavirus disease 2019 (COVID-19) is defined as illness caused by a novel coronavirus called severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2; formerly called 2019-nCoV), which was first identified amid an outbreak of respiratory illness cases in Wuhan City, Hubel Province, China. It was initially reported to the World Health Organization (WHO) on December 31, 2019 WHO. On January 30, 2020 the WHO declared the COVID-19 outbreak as a global health emergency, on March 11, 2020 the WHO declared COVID-19 a global pandemic, its first such designation since declaring H1N1 influenza a pandemic in 2009, (WHO) (1).

Symptoms of COVID-19 are variable, but often include fever, cough, headache, fatigue, breathing difficulties, and loss of smell and taste. Older people are at a higher risk of developing severe symptoms. Some people continue to experience a range of effects (long COVID) for months after recovery, and damage to organs was also observed. The virus is transmitted through respiratory droplets and airborne particles exhaled by an infected person. Those particles may be inhaled or may reach the mouth, nose, or eyes of a person through touching or direct deposition (i.e. being coughed on). The risk of infection is highest when people are in close proximity for a long time, but particles can be inhaled over longer distances, particularly indoors in poorly ventilated and crowded spaces (2).

Social isolation was the primary control of the infected person. The social isolation and potential risk of fatal complications of the virus caused behavioral changes and mental health issues among survivors (3). Previously reported studies have shown that loneliness experienced during isolation was the primary cause of the depression and anxiety after recovery from acute infection. However, there was limited literature available on the recovery of symptoms along with the perception of survivors about their disease. Thus this study was designed to evaluate long term sequlae of the COVID-19 and their perception about the disease.

MATERIALS AND METHODS

This was a cross sectional descriptive study conducted by using a questionnaire. A snowball sampling method was used to identify the participants. The patients with PCR positive COVID-19 were included in this study between 18 to 60 years of age. There was no gender restriction on the study population. Those patients experiencing anxiety, depression and respiratory problems before diagnosis of COVID-19 were excluded. The data was collected from 5 April to 5 June 2021. This Study was conducted at Royal College of Nursing, Swat, Pakistan.

DATA COLLECTION INSTRUMENT

For data collection, five point Likert scale questionnaire was designed according to the objectives of the study. The questionnaire included questions related to the experience of COVID-19 symptoms after recovery and perception of the COVID related restrictions.

DATA ANALYSIS:

The data was analyzed using SPSS version 22.0. The responses of the series of questions on Likert scale are presented in the form of pie charts.

RESULTS

A total of 90 perticipants were included in this study, out of which 45 were qualified nurses, 27 were students and 19 were non nursing population. Regarding long term symptoms and mental health issues summary of responses is given in Figure 1(a-g). After recovering 18% were experiencing breathing problems (Figure 1-a), 15% had fever (Figure 1-b), 9.5% had loss of taste and smell (Figure 1-c), 10.7% had gastrointestinal problems (Figure 1-d), 14.1% contuned to have sleep disorders (Figure 1-e), memory loss was reported in 5% (Figure 1-f) and 8.5% has sadness and mood swings (Figure 1-g).

Figure 1-a. Q1. Do you experience breathing problem after recovery (n=83)

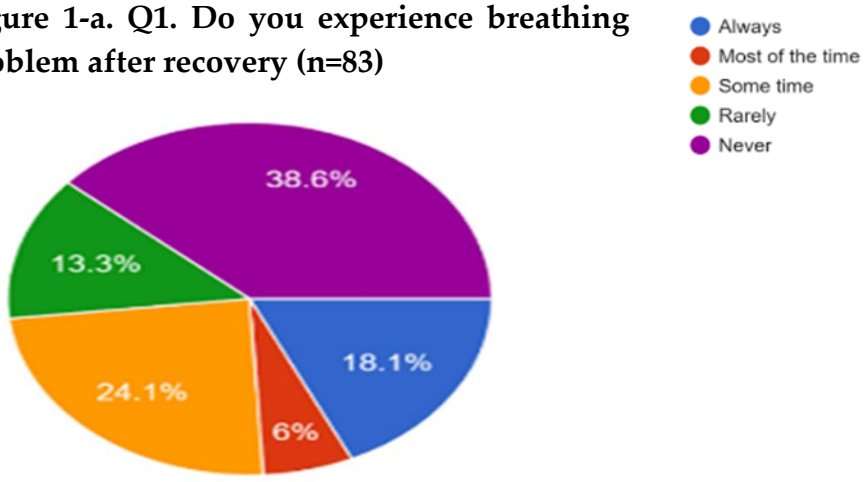


Figure 1-b. Q2. Do you experience fever after recovery (n=83)

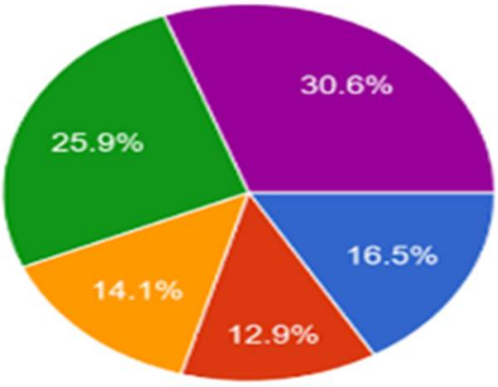


Figure 1-c. Q3. Do you experience loss of taste or smell after recovery (n=84)

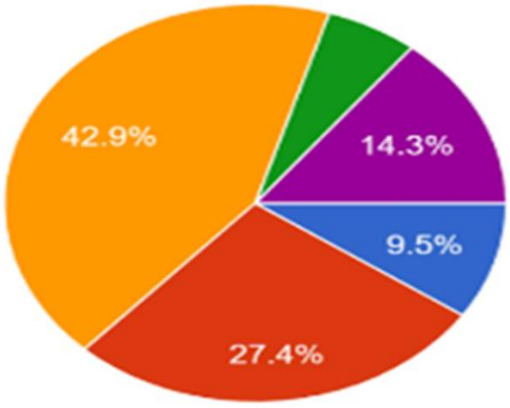


Figure 1-d. Q4. DO you feel vomiting or any other gastrointestinal problem after recovery (n=84)

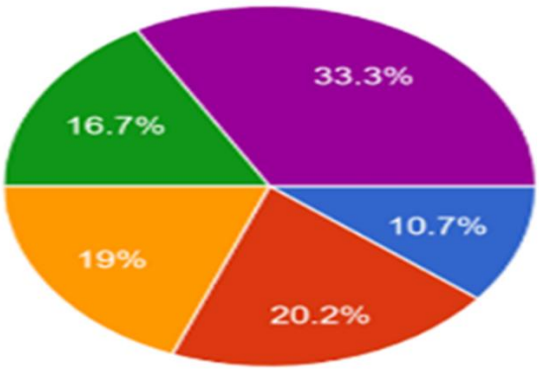


Figure 1-e. Q5. Do you experience sleep disturbance after recovery (n=85)

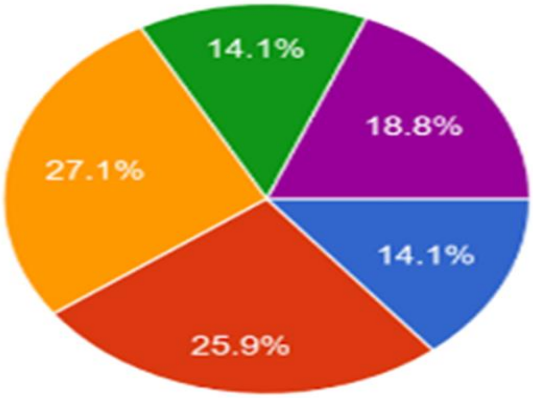


Figure 1-f. Q6. Is there any loss of memory you experienced after recovery (n-83)

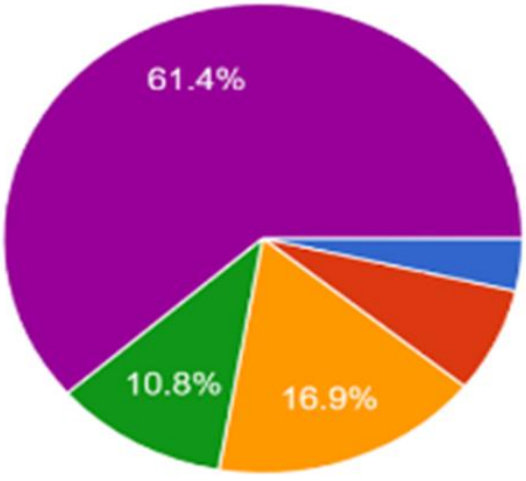
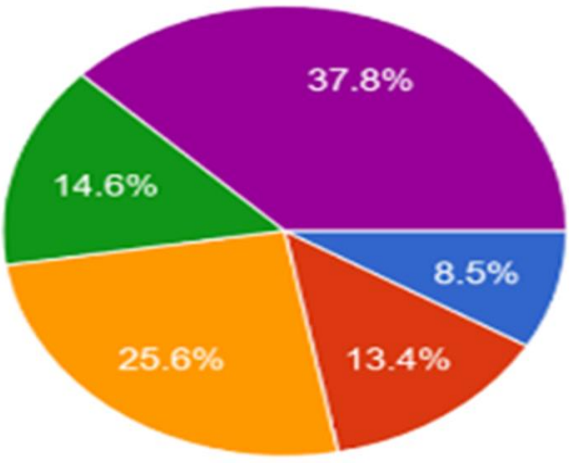


Figure 1-g. Q7. Do you experience sadness and mood swings after recovery (n=82)



Regarding perception of the participants great majority denied about spread of COVID-19 in social gatherings (Figure 2-a). Great majority also considered social isolation as a triger for anxiety and depression (Figure 2-b), they also believed that lockdown was useful in control of the disease (Figure 2-c), symptoms were severe among smokers (Figure 2-d) and pandemic has increased poverty (Figure 2-e).

Figure 2-a. Q1. COVID-19 affects our social gatherings even after recovery (n=83)

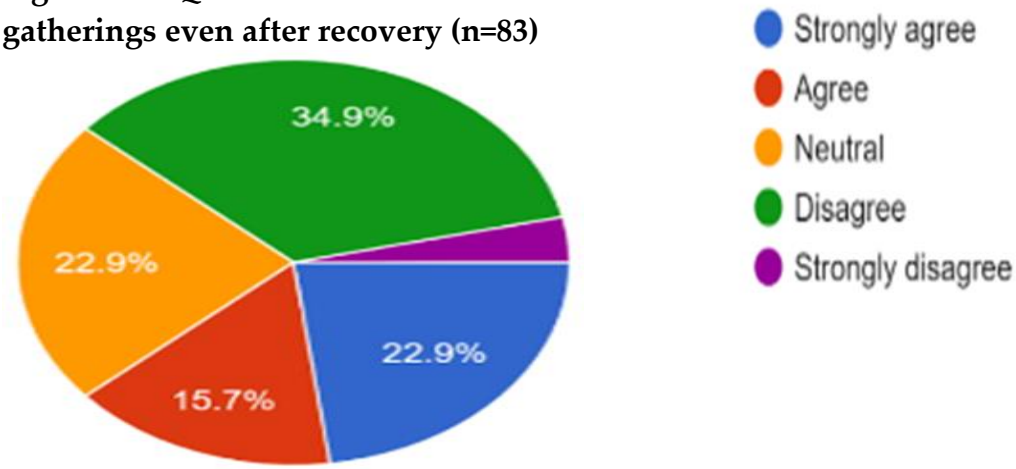


Figure 2-b. Q2. social isolation during COVID triggers anxiety and depression after recovery (n=83)

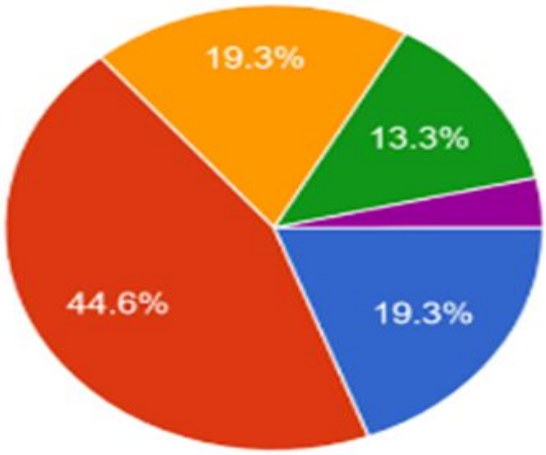


Figure 2-c. Q3. Lockdown and restrained social gatherings helped in controlling spread of COVID 19 (n=83)

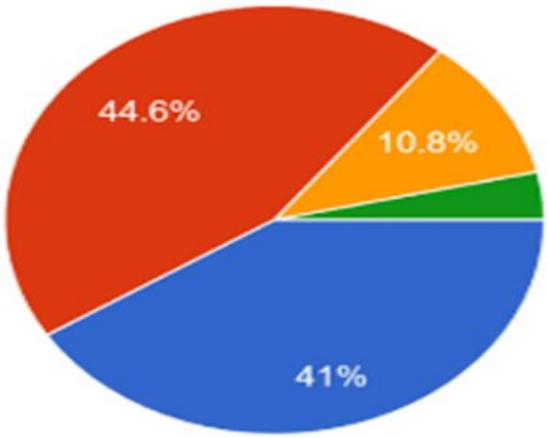


Figure 2-d. Q4. Severity of COVID 19 symptoms was higher among smokers (n=82)

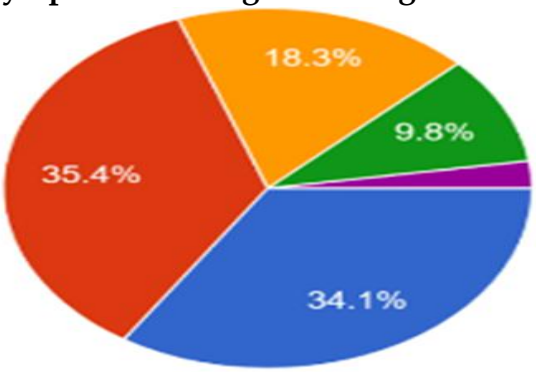
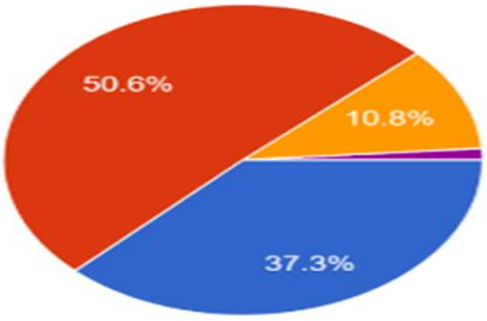


Figure 2-e. Q5. COVID- 19 pandemic has increased poverty in developed countries (n=83)



DISCUSSION

The study showed that majority of the patients experience some kind of long term effects of COVID-19 after apparently complete recovery. These problems not only involve their long term symptoms but also there is a risk of mental health issues, such as anxiety and depression. However great majority considered that the control of the disaese was possible because of lockdown. They also believed that pandemic has brought a height of inflation resulting in poverty. The COVID-19 was a global pandemic and all nations were affected without any

exception. Recent research has reported long term sequelae of the symptoms and also mental health issues thus in general over results are consistent with the available literature (4-5).

A cross-sectional survey research was conducted the United Kingdom regarding loneliness in the UK during covid- Their results showed the prevalence of loneliness was 27% (530/1964). Risk factors for loneliness on younger age group reproted as being separated or divorced, greater emotion regulation difficulties, and poor quality sleep due to the COVID-19 crisis. On the other hand higher levels of social support such as the cases of being married/co-habiting and living with other family members were protective factors (6). Another study was reported from China regarding the mental health of general population during the Covid-19. There were 1738 respondents from 190 Chinese cities. This study found that moderate-to-severe stress, anxiety and depression were noted in 8.1%, 28.8% and 16.5%, respectively and there were no significant longitudinal changes in stress, anxiety and depression levels (7).

Another study was conducted in Italy, reported that the patients with mild cognitive impairment and Alzheimer's disease were among the most affected in the early stages of the COVID-19 pandemic due to the direct effects of the virus and by indirect effect due to health care delivery (8). This insteretsing finding as most of the healthcare facilities were directed to the virus, and patients with chronic illneses suffered indirect effects due to shortage of doctors and health care providers. Sleep disturbaces were reported in patients and some of the continued to experience it afterwards. This may be experienced as part of anxiety and depression or might be other way round where it is causing depression. Further studies are required to expmore it further.

Pakistan being the 3rd world country,, and with COVID poverty increased drastically, respondents were seen showing strong agreement on that. However inflation has been observed globally (9). Research confirmed that people tended to respond to emergencies such as stress or death in the way of religion, which can comfort tense moods and bring more positive emotions (10). However explorng coping strategies is beyond the scope of this study. Similar to our exploration, China did a research during the initial outbreak of COVID-19 as it was firstly originated from China so they were the first one to act promptly (11). Their study was to explore the impacts of COVID-19 on people mental health, to assist policy maker to develop actionable policies, and help clinical practitioners (e.g., social workers, psychiatrists, and psychologists) provide timely services to affected populations. They collected their sample and analyze the Weibo posts from 17,865 active Weibo user using the approach of Online Ecological Recognition (OER) based on several machine-learning predictive models. They calculated word frequency, scores of emotional indicators (e.g., anxiety, depression, indignation, and Oxford happiness) and cognitive indicators (e.g., social risk judgment and life satisfaction) from the collected data (11). The results showed that negative emotions (e.g., anxiety, depression and indignation) and sensitivity to social risks increased, while the scores of positive emotions (e.g., Oxford happiness) and life satisfaction decreased (11). The rate of anxiety increased among all because people were concerned more about their health and family, while less about leisure and friends. The results contribute to the knowledge gaps of short-term individual changes in psychological conditions after the outbreak (12).

The data was collected from a small set of participants, majority of them belonged to nursing profession, thus they were aware of the disease pattern, thus their mental health might not have affected to that extent. However a large scale study including general population would be more appropriate to answer mental health issues in post-COVID patients and to understand long term sequelae of the survivors.

CONCLUSION

In conclusion the study population has shown long term effects of COVID-19 in terms of persistent symptoms or mental health issues. Majority of the survivors agreed that the pandemic has brought poverty. Further long term studies are required to explore these questions further.

CONFLICT OF INTEREST:

Authors declare no conflict of interest

FUNDING SOURCE:

The study did not receive any external funding

ETHICAL APPROVAL:

The study was approved by local Research Ethics Committee.

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Case Report

A COMPLEX CASE OF AUTOIMMUNE ENCEPHALITIS WITH RENAL TWIST - A CASE REPORT

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ABSTRACT

Autoimmune Encephalitis (AE) presents diagnostic challenges due to its diverse symptoms. We describe a case of a 32-year-old male with fever, seizures, and altered mental status, presented at Aga Khan hospital, Karachi, Pakistan. Unusual cerebrospinal fluid findings and autoimmune markers led to AE diagnosis. Autoimmune encephalitis's intersection with lupus nephritis required a multidisciplinary approach, resulting in significant improvement. This case highlights the importance of clinical suspicion and antibody testing in AE diagnosis and offers insights into evolving autoimmune disease management.

Key Words: Autoimmune Encephalitis, Lupus Nephritis, Multidisciplinary Approach

INTRODUCTION

Autoimmune Encephalitis (AE) is a dynamic and complex neurology subspecialty marked by cerebral inflammation due to an immune response against neural antigens, presenting with a spectrum of neurological symptoms, including altered mental status, seizures, and cognitive deficits (1). Autoimmune encephalitis can manifest independently or as part of systemic autoimmune disorders like systemic lupus erythematosus (SLE), impacting multiple organ systems, including the central nervous system (CNS) (2). Lupus nephritis, a prominent renal manifestation in SLE, presents an intriguing challenge for clinicians in navigating the complex relationship between autoimmune diseases and their impact on the nervous system (3). Around 1,000 cases of AE reportedly occur annually in United Kingdom, and despite its challenging course, effective treatment can lead to substantial recovery (4).

Case Presentation

A previously healthy 32-year-old male presented to a private tertiary care hospital with altered sensorium, seizures, and fever following a five-day history of fever, rigors, and chills. Initially treated at a local clinic with intravenous hydration and antimalarial treatment, his condition worsened, leading to irritability, disorientation, and a low Glasgow Coma Scale (GCS). He was subsequently intubated at another local private hospital, where cerebrospinal fluid (CSF) analysis confirmed meningoencephalitis, prompting transfer to a private tertiary care hospital for advanced care.

Case History

Upon admission to a private tertiary care hospital, a comprehensive diagnostic workup was initiated to evaluate the patient's condition further. Initial investigations included CSF studies, computed tomography (CT) head, and magnetic resonance imaging (MRI) head. The CSF analysis revealed several notable findings, including an elevated white blood cell count indicative of pleocytosis, a high protein

concentration, and a decreased glucose concentration. These CSF findings were highly suggestive of a central nervous system infection.

The CT and MRI scans of the patient's head showed no intracranial hemorrhage, infarct, or mass lesions, ruling out no structural brain abnormalities. Given the complexity of the case, an autoimmune workup was subsequently initiated. This workup revealed positive results for several autoimmune markers, including Antinuclear Antibodies (ANA), Anti-Ro antibodies, Anti-Scl antibodies, and Anti-Double-Stranded DNA (ADNA) antibodies.

The patient's generalized tonic-clonic seizures (GTCs) were managed in consultation with the neurology team, who prescribed appropriate anti-epileptic drugs tailored to the patient's needs. Additionally, the rheumatology team was consulted to address the autoimmune markers detected, and the patient received pulse steroid therapy as part of the autoimmune management plan.

Furthermore, the patient developed acute kidney injury (AKI) with high anion gap metabolic acidosis (HAGMA), necessitating a nephrology consult. Comprehensive nephrological evaluation and management were initiated promptly.

After four days of intensive care and specialized treatment, the patient's condition improved, allowing for successful weaning from ventilator leading to extubation. Subsequently, the patient was transferred to a medical ward for ongoing care and further monitoring.

Physical Examination

On arrival in the ER, GCS was 2/10, and the patient was intubated and on AC/ VC mode of ventilation with a respiratory rate of 18 per minute, tidal volume of 450 per minute, and FiO2 of 50%. His blood pressure was 100/50 mmHg, Pulse was 73 per minute, and temperature was 37˚F. Pupils were bilaterally equally reactive. Skin was intact. The chest was clear, and no adventitious sounds were heard. Nasogastric tube was placed and Ensure nutritional supplement started at 40cc per hour.

Differential diagnosis:

1. Tuberculosis Meningitis
2. Encephalopathy due to lupus cerebritis Or autoimmune Encephalitis
3. Acute Kidney injury due to lupus nephritis Or drug-induced.
4. Malaria
5. Seizures

Laboratory and diagnostic test findings with rationale

Based on the presented symptoms, several diagnostic measures can be employed to investigate autoimmune encephalitis or related risk factors. The initial assessment commonly encompasses a range of examinations, including blood tests and radiological evaluations such as chest X-rays, CT head, MRI, and EEG. A summary of the investigations is presented in Tables 1 and 2.

Table. 1 Summary of diagnostic procedures of the patient

Chest X-Ray	Haziness in the left lower zone with blunting of the left costophrenic angle suggests mild pleural effusion with underlying atelectasis.
MRI Brain	There was no evidence of acute infarction, hemorrhage, or mass effect. No meningeal or parenchymal enhancement. Incidental note of small right quadrigeminal cistern lipoma.
CT Head without contrast	No acute intracranial hemorrhage, established infarct, or mass effect.
EEG	Abnormal findings were suggestive of severe encephalopathy. Burst suppression pattern (burst of theta and delta activity with variable suppression). Intermittent generalized delta bursts.

Table. 2 Summary of laboratory investigations of the patient

Labs	Value	Labs	Value
Hb	11.7g/dl ← 9.1g/dl	BUN	17mg/dl ← 53mg/dl
Hct	37.0% ← 28.1%	Cr	1.1mg/dl ← 4.0mg/dl
RBC	4.09*10E12/L ← 3.22*10E12/L	eGFR	>60ml/min ← 15.12mL/min
WBC	15.9*10E9/L ← 10.5 *10E9/L	Na	150mmol/L ← 152mmol/L
Lymphocytes	16.0% ← 19.7 %	K	4.0mmol/L ← 3.8mmol/L
Platelets	294*10E9/L ← 291 *10E9/L	Cl	104mmol/L ← 116mmol/L
SGPT	151IU/L	Bicarb	22.5mmol/L ← 19.20mmol/L
Albumin	4.4g/dl	Anion Gap	18mmol/L
s. Ionized Calcium	4.89mg/dl	Mg	2.5mg/dl ← 2.9mg/dl
Phosphorus	3.8mg/dl	Glu. Random	118mg/dl
Plasma Ammonia	50ug/dl	S.p- ANCA S c-ANCA	8.26U/ml<0.3U/mL
CRP	33.20mg/L ← 118mg/L	S. Procalcitonin	0.14ng/mL
S.anti-dsDNA (IgG)	41.3 IU/ml	U1-RNP-Antibodies	2.50 U/ml
		SS-A/Ro Antibodies	59.21U/ml
		SS-B/La Antibodies	4.66 U/ml
		Sm-Antibodies	0.37 U/ml
		Scl-70 Antibodies	5.78 U/ml
S. Anti CCP	<8.0 U/mL	ANA Group test- Pattern	Coarse Speckled
		Estimated Endpoint Titer	1/5120
		Anti-smooth muscle Antibodies	negative
		Anti-mitochondrial Antibodies (AMA)	negative

Table 3. Summary of Blood Gases(Last time retrieved)

PH	7.45	7.38
PCO2	33.90mmHg	34.20mmHg
PO2	74.80mmHg	207.60mmHg
Bicarbonate	22.80	19.70mEq/L
Base Excess	-0.6mEq/L	-4.6mEq/L
O2 Sat	95.50%	99.70%

Management

The patient received immediate treatment, including empiric intravenous antibiotics and antiviral therapy, to address potential causes of meningoencephalitis. Anticonvulsant medications were administered for seizure control alongside mechanical ventilation in the ICU for support. There was a positive ANA test suggesting an autoimmune disorder, and CSF analysis did not identify any specific pathogen responsible for the central nervous system infection. Close monitoring managed fluctuating hypernatremia, with no recurrent seizures after 48 hours. Rheumatology initiated pulse steroid therapy for autoimmune markers, while nephrology addressed acute kidney injury (AKI) through comprehensive management.

This collaborative, multidisciplinary approach encompassed both autoimmune aspects and AKI-related complications. As the patient's condition improved, he was extubated and achieved a GCS score of 15/15, indicating full alertness and orientation. Subsequently, the patient transitioned from the ICU to a medical ward for continued monitoring. Over three days without complications, the patient's stability allowed for discharge, marking a positive outcome. The patient was discharged with the clear guidelines to continue taking all prescribed medications. The take-home medications included prednisolone 5m/tablet, Leviteracitam tablet 500 mg/tablet, Esomeprazole 40mg/capsule, Hydralazine HCL 25mg/tablet, and Pyridoxine HCL 50 mg/tablet. The patient looked happy and stable while he was going home.

Pharmacological Therapy

Several drugs were used to treat the patient's condition. Table 3 shows the typical medications used in the treatment plan for the patient.

DISCUSSION

Diagnosing AE is complex, and successful patient outcomes fundamentally depends on early detection and treatment (5). The background of diagnosing autoimmune Encephalitis (AE) has evolved, becoming increasingly feasible due to established consensus clinical criteria and the broader availability of antibody tests (6). A high index of suspicion is vital, especially when patients initially present with psychiatric symptoms. Diagnosis often relies on subsequent neurological manifestations and supportive evidence from tests and MRI, which can occasionally yield normal results.

Accurate diagnosis involves coordinating antibody testing with a neurologist and neuro-immunology laboratory, guided by clinical assessment. Establishing a syndromic diagnosis remains a viable option in cases without detectable antibodies.

Table 3. Medicines prescribed to the patient presenting with complex encephalitis

Medications	Classification	Mechanism of Action
Pyridoxine HCL	Vitamin (Vitamin B6)	A water-soluble vitamin acts as a coenzyme in amino acid, neurotransmitter, and glycogen metabolism.
Sodium Bicarbonate	Alkalinizing agent, antacid	Sodium bicarbonate is a systemic and urinary alkalinizing agent.
Prednisolone	Corticosteroid (Glucocorticoid)	Prednisolone, a synthetic corticosteroid, exerts anti-inflammatory and immunosuppressive effects by suppressing the immune response and inflammation in various conditions.
Metoclopramide HCL	Prokinetic agent, antiemetic	Metoclopramide, a dopamine receptor antagonist in the upper digestive tract, enhances gastrointestinal motility and manages nausea and vomiting.
Ondansetron HCL	Antiemetic	Selective 5-HT3 receptor antagonist alleviates nausea and vomiting by blocking serotonin receptors in the brain and gut.
Levetiracetam	Antiepileptic (Anticonvulsant)	Levetiracetam modulates neurotransmitter release by binding to synaptic vesicle protein 2A (SV2A) and is employed for seizure control in epilepsy.
Esomeprazole	Proton Pump Inhibitor	Esomeprazole inhibits the gastric proton pump (H+/K+ ATPase), reducing stomach acid secretion, and is prescribed for conditions involving excessive gastric acid, such as GERD.
Valproate Sodium	Antiepileptic (Anticonvulsant)	Valproate sodium modulates the brain neurotransmitter GABA, reducing abnormal electrical activity, and is indicated for epilepsy and bipolar disorder.
Dioctahedral smectite	Antidiarrheal, Adsorbent	Dioctahedral smectite, a clay-based adsorbent in the gastrointestinal tract, binds to toxins and pathogens, reducing diarrhea.
Artesunate	Antimalarial	Antimalarial disrupts malaria parasite growth and reproduction in red blood cells.
Hydralazine	Antihypertensive	Hydralazine induces vasodilation by relaxing blood vessel smooth muscle, lowering blood pressure, and treating hypertension.
Ethambutol	Anti-tuberculosis Agent	Ethambutol inhibits mycobacterial cell wall synthesis, disrupting arabinogalactan and the bacterial cell wall, and is employed in tuberculosis treatment.
Isoniazid+ Rifampicin	Antituberculosis Agents	Isoniazid disrupts mycobacterial cell wall synthesis, while rifampicin inhibits bacterial RNA synthesis; combined, they are highly effective against tuberculosis.
Calcium Gluconate	Calcium Supplement	Calcium gluconate supplements calcium, treats deficiency, and stabilizes cardiac membrane potential in hyperkalemia.

Although CSF findings frequently reveal abnormalities in AE, including a mild lymphocyte increase and moderately elevated CSF protein levels, it's essential to note that up to one-third of patients may present entirely unremarkable CSF results, and this should not exclude the possibility of the diagnosis (4). The standard therapy for systemic lupus erythematosus and lupus nephritis (LN) initially

involved high-dose corticosteroids, which improved 5-year survival rates for proliferative LN to 55%. However, prolonged corticosteroid use had adverse effects, including renal failure. In the 1970s, the addition of cytotoxic agents like cyclophosphamide raised 5-year survival rates to 80%. Despite this improvement, treatment failures remained common, and end-stage renal disease (ESRD) progression risk remained high(7).

CONCLUSION

In conclusion, this case underscores the complexity of diagnosing autoimmune encephalitis, emphasizing the importance of a high index of suspicion, clinical evaluation, and antibody testing. It highlights the multidisciplinary approach required for comprehensive patient care involving neurology, rheumatology, and nephrology. Additionally, it provides insights into the evolving treatment landscape, moving from corticosteroids to cytotoxic agents in lupus nephritis management. This case contributes to our understanding of AE, offering valuable lessons for improved diagnosis and patient outcomes.

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