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Curriculum in Medical Education: Blueprint, Contract, or Living System?

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The Educational Covenant: Beyond the Syllabus

Is medical training merely a fixed list of topics to be learned, or is it better understood as the social contract — in effect, the constitution — that exists among the academy, the student, and the patient? The curriculum functions as the unspoken architect of the professional character within the complex environment of modern healthcare. It is more than a means of dispensing knowledge; it shapes the future clinical judgment and moral strength of tomorrow's physicians [1,2]. In a country like Sudan, this educational blueprint takes on particular urgency. In an environment marked by a shifting resource base, periods of national strife, and a pressing need for institutional change, the curriculum can no longer remain a static artifact of the past.

Instead, it should function as a dynamic, responsive system — one that enables healthcare professionals to practice effectively under extreme pressure, so that the promise of quality care endures despite a turbulent environment [3,4].

The Invisible Architecture

To fully understand the development of medical education, we must move beyond a reductionist view of the curriculum as a mere set of course descriptions. Historically, it has been regarded as a syllabus — a fixed body of material transmitted from teacher to student. The contemporary view, by contrast, treats the curriculum as the aggregate of intended learning experiences: the how and why of medicine, conveyed through deliberate pedagogical design and clinical rotations aimed at building genuine competence [5].

At its most fundamental level, the curriculum represents a social contract among three spheres:

The institution, which promises a well-organized, quality learning environment and valid certification.

The learners, who commit to the challenges of the profession in pursuit of a clear pathway to mastery.

- Society, which grants the university the authority to teach, on the condition that graduates are safe, culturally competent, and responsive to the country's specific health needs.

The Governance of Learning: A Shift in Power

Curriculum determination was historically top-down and faculty-centered. A significant shift toward a stakeholder-driven model is now under way. In Sudan, regulatory authorities such as the Ministries of Higher Education and the Sudan Medical Council act as guardians of standards, ensuring that local degrees remain aligned with international benchmarks [6]. At the same time, faculty senates and academic councils serve as the working architects, using curriculum

mapping to align disparate subjects with overall graduation objectives [7].

Increasingly, student voice has become an important contributor to this process; student feedback helps ensure that the lived curriculum genuinely reflects the planned curriculum [8]. Social accountability further requires that the specific health needs of the Sudanese population remain the core guiding principle behind university learning outcomes.

The Architects and Criteria of Design

Development of a modern curriculum is an interdisciplinary collaboration among specialist commissions, medical education experts, and instructional designers. Constructive alignment — ensuring that learning activities and assessments correspond directly to intended learning outcomes — is a principle essential to success [9].

Curriculum design must satisfy criteria at several levels. Competency frameworks such as CanMEDS and Bloom's Taxonomy provide the educational scaffolding [10,11]. At the societal level, priority should be given to Sudan's specific disease burden, such as

maternal health and tropical medicine. At the institutional level, local faculty capacity and infrastructure must be considered. At the international level, alignment with World Federation for Medical Education (WFME) standards is necessary for global recognition [6,12].

The great Transition: From “Knowing” to “Doing”

Table 1. Comparison Between Traditional and Modern Integrated/Competency-Based Medical Education (CBME) Models

Dimension	Traditional Model	Modern Model (Integrated/CBME)
Focus	Teacher-centered	Student-centered
Structure	Fragmented / Siloed	Integrated
Assessment	Knowledge recall	Competency and performance
Flexibility	Rigid	Adaptive

Traditional discipline-based medical education is increasingly being replaced by integrated, competency-based medical education [13]. In making this shift, institutions must remain alert to the Hidden

Curriculum — the professional values and ethics that students absorb through observation of institutional and hospital culture [14]. These unscripted lessons in resilience and resourcefulness are as essential in conflict-affected settings as formal clinical knowledge.

Future Directions: Toward 2030

Several developments over the coming decade are non-negotiable:

Digital and hybrid models: use of learning management systems (LMS) to sustain educational continuity during crises.

AI integration: moving beyond technology adoption toward genuine AI literacy that supports ethical clinical decision-making [15].

Interprofessional education (IPE): promoting shared learning among medicine, nursing, and pharmacy to reflect real-world clinical teams [16].

Community-oriented focus: shifting clinical training toward rural and primary healthcare settings where it is most needed.

Conclusion: A Living Covenant

The medical curriculum is not merely a document but a living contract and a future strategy [1,13]. It is the blueprint for the physicians who will lead Sudan's eventual recovery. Urgent reform, multidisciplinary cooperation, and context-sensitive innovation are called for.

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High-Resolution Ultrasonographic Evaluation of Median Nerve Morphological Alterations in Patients with Type 2 Diabetes Mellitus: A Controlled Cross-Sectional Study

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Diabetic peripheral neuropathy (DPN) is a frequent and debilitating complication of diabetes mellitus (DM), significantly impacting patients' quality of life. High-resolution ultrasonography (HRUS) has emerged as a promising non-invasive tool for assessing morphological changes in peripheral nerves.

The objective was to evaluate the morphological alterations of the median nerve in patients with Type 2 Diabetes Mellitus (T2DM) compared to healthy controls using HRUS and to correlate these changes with the duration of diabetes.

A controlled cross-sectional study was conducted involving 200 participants (100 diabetic patients and 100 healthy controls). Ultrasound examination of the median nerve was performed at the carpal tunnel inlet using a 12–15 MHz linear transducer. The cross-sectional area (CSA) was measured using the continuous tracing technique. Statistical analysis included independent t-tests, Pearson correlation, one-way ANOVA for duration groups, multiple linear regression, and ROC curve analysis.

The mean CSA of the median nerve was significantly higher in diabetic patients compared to the control group ($p < 0.001$). In the right wrist, the mean CSA was $0.1171 \pm 0.0243 \text{ cm}^2$ for cases vs. $0.0915 \pm 0.0549 \text{ cm}^2$ for controls. In the left wrist, it was $0.1179 \pm 0.0235 \text{ cm}^2$ for cases vs. $0.0847 \pm 0.0182 \text{ cm}^2$ for controls. One-way ANOVA revealed significant differences in CSA across diabetes duration groups ($F = 18.42, p < 0.001$). A moderate positive correlation was found between CSA and diabetes duration ($r = 0.46, p < 0.001$). Multiple linear regression identified diabetes duration as the strongest predictor of increased CSA ($\beta = 0.41, p < 0.001$). ROC analysis yielded an AUC of 0.86, with an optimal cut off of 10.5 mm^2 (0.105 cm^2) providing 82% sensitivity and 78% specificity.

High resolution ultrasound effectively detects median nerve enlargement in T2DM patients. These morphological changes correlate with disease duration, suggesting that HRUS can serve as a valuable biomarker for the early detection and monitoring of diabetic neuropathy.

Introduction

Diabetes mellitus (DM) is a chronic metabolic disorder characterized by persistent hyperglycemia, which leads to various

microvascular and macrovascular complications (1). Among these, diabetic peripheral neuropathy (DPN) is one of the most common, affecting approximately 30% to 50% of individuals with diabetes (2). DPN often manifests as sensory loss,

neuropathic pain, and, in advanced stages, can lead to foot ulceration and amputation (3)

Traditionally, nerve conduction studies (NCS) have been the gold standard for diagnosing DPN. However, NCS primarily assesses the functional integrity of large myelinated fibers and may not capture early structural changes (4). High-resolution ultrasonography (HRUS) has recently gained attention as a complementary diagnostic tool. HRUS allows for the direct visualization of nerve morphology, including changes in the cross-sectional area (CSA), fascicular pattern, and vascularity (5).

Studies have consistently shown that peripheral nerves, including the median nerve, tend to enlarge in diabetic patients even before the onset of clinical symptoms (6). This enlargement is thought to result from polyol pathway activation, leading to endoneurial edema and axonal swelling (7). This study aims to quantify the morphological alterations of the median nerve in T2DM patients using HRUS and to investigate the relationship between these changes and the duration of the disease.

Materials and Methods

This controlled cross-sectional study was conducted at Port Sudan City Hospitals between 2025 and 2026 and enrolled 200 participants: 100 patients with confirmed Type 2 Diabetes Mellitus (cases group) and 100 age- and sex-matched healthy individuals (control group). Eligibility criteria for cases included adults aged 30 to 70 years with a confirmed diagnosis of T2DM and willingness to provide informed consent. Exclusion criteria comprised a history of wrist trauma or carpal tunnel surgery, systemic conditions associated with neuropathy (such as chronic renal failure or vitamin B12 deficiency),

pregnancy, and clinical signs of inflammatory or hereditary neuropathies.

All participants underwent ultrasound examination of the median nerve using a Mindray Diagnostic Ultrasound System (Model DC-30, Appendix 1) and Model DC-8EXP (Appendix 2), each equipped with a high-frequency linear transducer (10-15 MHz). The examination was performed with the participant seated, the forearm supinated, and the wrist in a neutral position. The median nerve was identified in the transverse plane at the inlet of the carpal tunnel, using the pisiform bone and the scaphoid tubercle as anatomical landmarks.

The CSA of the median nerve was measured using the continuous tracing method, following the inner border of the hyperechoic epineurium. To ensure accuracy and reproducibility, three separate measurements were taken for each wrist, and the average value was recorded in square centimeters (cm²).

Data were analyzed using SPSS software. Descriptive statistics were used to summarize the demographic and clinical characteristics. Independent t-tests were employed to compare the mean CSA between the two groups. One-way Analysis of Variance (ANOVA) was used to compare the mean CSA across the four diabetes duration groups, followed by Tukey's HSD post-hoc test. Pearson correlation was used to assess the relationship between CSA and the duration of diabetes. Multiple linear regression analysis was performed to identify independent predictors of nerve enlargement. Receiver Operating Characteristic (ROC) curve analysis was conducted to determine the diagnostic accuracy and the optimal cutoff value for CSA. A p-value < 0.05 was considered statistically significant.

Results

The study population consisted of 200 participants. The mean age of the diabetic group was 54 ± 9 years, while that of the control group was 52 ± 8 years, with no significant differences in age or sex distribution between the two groups ($p > 0.05$).

The mean CSA of the median nerve was significantly larger in the diabetic group than in the control group for both the right and left wrists ($p < 0.001$), as shown in Table 1 and Figure 1.

Table 1: Comparison of Mean Cross-Sectional Area (CSA) Between Study Groups

Measurement Site	Group	Mean CSA $\pm$ SD (cm ²)	p-value
Right Wrist	Control	0.0915 $\pm$ 0.0549	<0.001
	Cases	0.1171 $\pm$ 0.0243	
Left Wrist	Control	0.0847 $\pm$ 0.0182	<0.001
	Cases	0.1179 $\pm$ 0.0235	

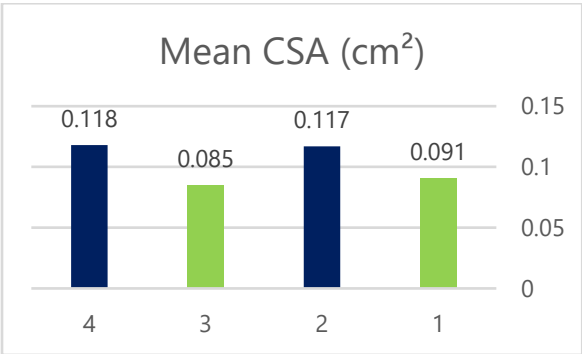


Figure 1: Comparison of Mean Cross-Sectional Area (CSA) Between Study Groups

Among the diabetic participants, the majority had long-standing disease: 34% had diabetes for more than 15 years, while only 12% fell within the 1-5 year range (Table 2).

Table 2: Distribution of Diabetes Duration Among Participants

Duration of Diabetes	Frequency (N=100)	Percentage (%)
1 – 5 Years	12	12%
6 – 10 Years	29	29%
11 – 15 Years	25	25%
>15 Years	34	34%
Total	100	100%

A moderate positive correlation was observed between median nerve CSA and diabetes duration ($r = 0.46$, $p < 0.001$), indicating progressive nerve enlargement with longer disease duration. Multiple linear regression analysis further identified diabetes duration as the strongest independent predictor of increased CSA ($\beta = 0.41$, $p < 0.001$), as shown in Table 3.

Table 3: Multiple Linear Regression Analysis for Predictors of Median Nerve CSA

Variable	Unstandardized B	Std. Error	Standardized β	t	p-value
Constant	0.082	0.009		9.11	<0.001
Diabetes Duration	0.003	0.0007	0.41	4.28	<0.001
Age	0.0002	0.0001	0.15	1.62	0.108

A one-way ANOVA was conducted to determine whether the mean CSA of the median nerve differed significantly according to diabetes duration. The results showed a statistically significant difference between groups ($F(3, 96) = 18.42, p < 0.001$), as shown in Table 4.

Table 4: One-Way ANOVA Comparison of Median Nerve CSA by Diabetes Duration

Source of Variation	Sum of Squares	df	Mean Square	F	p-value
Between Groups	0.0452	3	0.0151	18.42	<0.001
Within Groups	0.0787	96	0.00082		
Total	0.1239	99			

The ROC curve for median nerve CSA in predicting diabetic changes showed an area under the curve (AUC) of 0.86. The optimal cutoff value was identified as 10.5 mm² (0.105 cm²), yielding a sensitivity of 82% and a specificity of 78% (Figure 2).

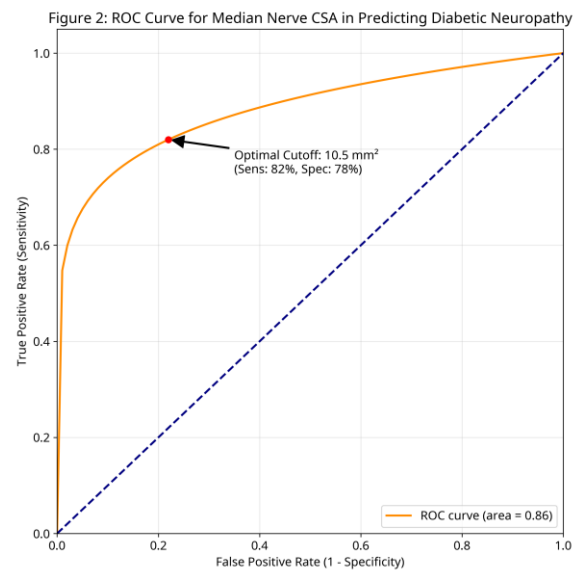


Figure 3: A 57-year-old woman with a 7-year history of diabetes mellitus. The median

nerve cross-sectional area shows a marked difference between the right and left sides, within the normal range (0.12 cm² right, 0.06 cm² left wrist), with a normal fascicular pattern and echogenicity bilaterally.



Figure 4: A 47-year-old man with a 5-year history of diabetes mellitus. The median nerve cross-sectional area shows a marked difference between the right and left sides (0.10 cm² right, 0.07 cm² left wrist), with preserved fascicular pattern and echogenicity bilaterally.

Discussion

The findings of this study demonstrate a significant increase in median nerve CSA in patients with Type 2 Diabetes Mellitus compared with healthy controls. These results

are consistent with previous literature suggesting that peripheral nerve enlargement is a characteristic feature of diabetic neuropathy (8). This enlargement is a hallmark of DPN and is believed to result from a complex interplay of metabolic and microvascular factors (9,10). The observed increase in median nerve CSA in diabetic cases, even in the absence of overt clinical symptoms, aligns with studies suggesting that HRUS can detect subclinical nerve changes earlier than traditional nerve conduction studies (NCS) (11,12).

The pathophysiology of nerve enlargement in diabetes is multifactorial. Chronic hyperglycemia leads to the activation of the polyol pathway, resulting in the accumulation of sorbitol and fructose within the nerve fibers. This creates an osmotic gradient that draws water into the endoneurium, leading to edema and subsequent increases in CSA (9). Additionally, microvascular changes and non-enzymatic glycation of nerve proteins contribute to structural remodelling and thickening of the nerve sheaths (13,14).

Our analysis of median nerve echogenicity revealed a shift towards reduced echogenicity (hypoechoic appearance) in diabetic patients, particularly in more advanced stages. This finding is consistent with studies linking reduced echogenicity to increased water content and structural disorganization within the nerve due to edema and demyelination

(13,15). While our study did not specifically quantify vascularity, the presence of increased vascularity in diabetic nerves, as reported in other HRUS studies, further supports the notion of microvascular dysfunction in DPN (16,17).

Our study also highlighted a significant positive correlation between the duration of diabetes and the degree of nerve enlargement. This suggests that the cumulative metabolic insult over time leads to progressive morphological changes in the peripheral nerves. Similar findings have been reported by Watanabe et al., who noted that nerve CSA increases linearly with the duration of the disease (18).

The high diagnostic accuracy observed in our ROC analysis ($AUC = 0.86$) supports the use of HRUS as a reliable tool for identifying diabetic nerve alterations. A cutoff value of 10.5 mm^2 was found to be highly effective in distinguishing diabetic cases from controls. This is slightly lower than cutoffs typically used for Carpal Tunnel Syndrome (often 12 mm^2), suggesting that diabetic nerve swelling is a generalized process that may occur independently of mechanical compression (19).

One limitation of this study is its cross-sectional design, which precludes definitive conclusions about the temporal progression of nerve changes. Future longitudinal studies are needed to determine whether HRUS-

detected changes can predict the future development of clinical neuropathy.

Conclusion

High-resolution ultrasonography is a sensitive and non-invasive modality for evaluating the morphological changes of the median nerve in diabetic patients. The significant enlargement of the median nerve and its correlation with disease duration indicate that HRUS can serve as an important imaging biomarker for the early detection and monitoring of diabetic peripheral neuropathy. Incorporating nerve ultrasound into routine diabetic care may facilitate earlier intervention and improved patient outcomes.

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Impact of Radiology Request Form Quality on CT Imaging Accuracy: A Clinical Evaluation

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Abstract

Computed tomography (CT) is indispensable for modern diagnosis and quantitative assessment of internal organs, adipose tissue, and skeletal muscle; however, it entails ionizing radiation exposure (typically ~16 mSv) with a measurable stochastic cancer risk, underscoring the need for careful justification and optimized workflows. Radiology Request Forms (RRFs) are the primary communication tool between referring clinicians and radiology services. Incomplete or inaccurate RRFs can compromise diagnostic interpretation, prompt unnecessary examinations, and increase preventable harm, including inadequate radiation protection in potentially pregnant patients and contrast-induced nephropathy (CIN) when renal status or allergy history is undocumented. This prospective, descriptive, cross-sectional study evaluated the completeness and accuracy of CT RRFs across five hospitals in Khartoum State, Sudan (Kuwaiti Specialized, Alsaaha Specialized, Fedail Hospital, Military and Medical Service Administration, and East Nile Hospital) from October 2022 to February 2023. All CT referrals during the study period were included (n=1001), with RRF data abstracted using a closed-ended master collection sheet/questionnaire and analyzed in SPSS v22 using descriptive statistics. The completion of key fields was variable: patient name was recorded in 99.3% of forms, age in 84.5%, gender in 61.8%, and examination date in 64%. The requested body part was specified in 99.8% of the cases, but only 54.5% contained a provisional diagnosis, and clinical history was provided in 71.2% of the cases. Safety-critical documentation was notably deficient, with allergy history present in only 17.5% of the cases and renal function testing in 39.4% of the cases. Among 400 female patients, the last menstrual period/cycle was recorded in 70%, with registrars showing the highest omission (35.9%) and the highest rate of missing clinical history (35.1%); specialists had the lowest incomplete clinical history (24.1%), while general practitioners had the lowest incomplete menstrual history (22.7%). This study indicated that physician rank did not meaningfully improve RRF quality, indicating a system-wide need for strengthened form-filling practices, standardized requirements, and improved clinician–radiology communication to enhance CT diagnostic accuracy and patient safety.

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Introduction

Computed tomography (CT) has become an indispensable imaging modality for the detailed evaluation of human tissue and organ structures and is widely utilized for both diagnostic and quantitative assessments (1,2). Despite its clinical utility, CT involves exposure to ionizing radiation, typically approximately 16 millisieverts (mSv), which carries a measurable stochastic risk of carcinogenesis (3–5). This risk necessitates stringent radiation protection measures, including justification and optimization of imaging procedures to minimize unnecessary exposure (3).

Radiology request forms (RRFs) serve as the primary communication conduit between referring clinicians and radiology departments, encapsulating critical patient information and clinical indications that underpin appropriate imaging utilization (6–8). The accurate and comprehensive completion of RRFs is essential to ensure diagnostic accuracy, optimize patient safety, and facilitate adherence to radiation protection principles (6,9). Incomplete or inaccurate RRFs can lead to inappropriate imaging requests, diagnostic errors, and increased patient risk, including inadequate radiation protection for vulnerable populations such as pregnant women and those with renal impairment (6,8,9).

Contrast-enhanced computed tomography (CT) imaging further underscores the

importance of detailed clinical information on RRFs. Intravenous iodinated contrast agents, while enhancing diagnostic yield, pose risks, such as contrast-induced nephropathy (CIN), particularly in patients with compromised renal function or multiple comorbidities (10,11). Accurate recording of allergy history, renal function, and essential clinical parameters on RRFs is essential to minimize these risks and facilitate the safe use of contrast agents (12).

Despite their critical role, global studies reveal persistent deficiencies in the completeness and accuracy of RRFs, with completion rates for key clinical fields varying widely and often falling below acceptable standards (8,13,14). Such gaps compromise diagnostic efficacy and patient safety, highlighting the need for systematic evaluation and improvement of RRF practices.

This study aimed to evaluate the completeness and accuracy of radiology request forms used for CT imaging across multiple healthcare institutions in Khartoum State, Sudan. We identified specific deficiencies and patterns in form completion.

Materials and Methods

Study Design and Duration

This prospective, descriptive, cross-sectional study was conducted at five healthcare facilities located in Khartoum State, Sudan, over a period of five months, from October 2022 to February 2023: Kuwaiti Specialized,

Alsaaha Specialized, Fedail Hospital, Military Hospital, and East Nile Hospital. Ethical approval was obtained from the radiology departments of all participating hospitals, and the study adhered to the ethical principles outlined in the Declaration of Helsinki for biomedical research involving human subjects.

Study Sampling

The study population included all patients who underwent computed tomography (CT) at the specified institutions during the study period, resulting in a total sample size of 1001. The inclusion criteria covered all CT referrals, regardless of patient demographics or clinical indications. However, CT scan requests referred from other institutions to our department, as well as radiology requests written on other types of request forms, such as lab or pharmacy requests, were excluded from the study.

Data Collection Method and Tools

Data were collected using a structured, closed-ended questionnaire designed specifically for this study to extract relevant clinical and demographic information from RRFs. The questionnaire captured variables, including patient biodata (name, age, and gender), clinical history, allergy status, renal function tests, last menstrual period (LMP) for female patients, provisional diagnosis, and details of the requested imaging procedure. To maintain confidentiality and encourage accurate reporting, all patients and referring physician identifiers were anonymized during data abstraction.

Data management and statistical analysis

Data management involved systematic entry into a computer-based database, followed by statistical analysis using the Statistical Package for the Social Sciences (SPSS) version 22 for Windows. Descriptive statistics were used to summarize the data, with variables presented as frequencies and percentages to illustrate the completeness and accuracy of RRF components across institutions. Comparative analyses based on physician rank and other relevant subgroups were also conducted to identify patterns in form completion.

Results

Table 1 presents the proportion of biographical data completed by RRFs. Nearly all forms (99.3%) included the patient’s name, and 84.5% included the patient’s age. Sex was specified in 61.8% of the cases, whereas the examination date was noted in 64% of the cases. Moving beyond biographical details, Table 2 presents the completion rates for the various components of the medical records. The body part for which a CT scan was requested was specified in 99.8% of the forms; however, only 54.5% of the forms included a preliminary diagnosis. Clinical history was documented in 71.2% of the forms, and 70% recorded the date of the patient’s last menstrual cycle. However, laboratory tests, particularly renal function tests, were documented in only 39.4% of the cases, whereas the lowest percentage (17.5%) was observed for recording allergy history. Focusing on physician rank, Table 3 shows

that information regarding the last menstrual period (LMP) was most often provided in forms referred to by general practitioners, followed by specialists. However, registrars had the highest rate of missing LMP details. Regarding the completion of clinical history, Table 4 reveals that forms referred by

Table 1: Biodata information

	Completion Rate
Name	99.3%
Age	84.5%
Gender	61.8%
Examination Date	64%

registrars showed the most deficiencies in clinical history completion. Although specialists had the lowest frequency of incomplete clinical history, the difference between specialists and general practitioners was relatively small.

Table 2: Clinical information

	Completion Rate
Body Part Requested for Procedures	99.8%
Patient Clinical History	71.2%
Allergic History	17.5%
Last Menstrual Period	70%
Lab Tests (Renal Function Test)	39.4%
Provisional Diagnosis	54.5%

Table 3: Last Menstrual Period (LMP) Section Completion by Physician Rank

Physician Rank	LMP	
	Incomplete	Complete
General Practitioner	10	34
Registrar	59	105
Specialist	51	141
Total	120	280

Table 4: Clinical History Section Completion by Physician Rank

Physician Rank	Clinical History	
	Incomplete	Complete
General Practitioner	38	105
Registrar	137	253
Specialist	113	355
Total	288	713

Discussion

Ensuring the accuracy and comprehensiveness of RRFs for CT imaging is essential, as the clinical information they contain directly influences diagnostic accuracy and patient safety. However, incomplete RRFs remain a global issue, with completion rates varying widely across regions and institutions(6). Studies have reported completion rates ranging from as low as 26.67% to 89.1%, highlighting persistent deficiencies that can lead to up to 20% of radiographic examinations being diagnostically inadequate, potentially causing unnecessary radiation exposure (6). Accurate patient identification, beginning with the patient's full name, and inclusion of biodata such as age and gender are critical for proper record-keeping and interpretation. This study found high completion rates for patient names (99.3%) and age (84.5%), but lower rates for gender (61.8%) and referral date (64%), reflecting inconsistent adherence compared to previous research (15,16). The clinical history, which is important for the diagnosis and treatment, was completed in

71.2% of forms in our study, which is higher than in some reports but lower than in others (6,17). Alarminglly, allergy history was recorded in only 17.5% of cases, and renal function tests in 39.4%, both of which are essential for preventing adverse reactions, such as contrast-induced nephropathy. Among female patients, 70% of forms included last menstrual period (LMP) data, a key factor for radiation protection, with registrars showing the highest incomplete rates for LMP and clinical history sections (Tables 3 and 4). These findings align with prior studies showing variability in form completion across physician ranks and specialties (18). Another study conducted in Pakistan indicated that the last menstrual period (LMP) was not mentioned. (13) Advances in computed tomography (CT) technology and increasing imaging complexity underscore the growing need for thorough clinical information to enhance diagnostic accuracy(19). Detailed histories reduce missed diagnoses and improve radiologist confidence, with evidence showing mixed effects on reporting times but

consistent improvements in diagnostic precision ranging from 8% to 12% (20).

RRFs also play an important role in justifying radiographic examinations by ensuring that ionizing radiation is used only when clinically warranted. Justification requires evaluating the balance between clinical benefit and radiation risk and relies heavily on the completeness of referral information (21). However, high rates of unjustified imaging persist; for example, a Queensland audit found that over 75% of emergency X-ray requests initially lacked justification, with nearly half remaining unjustified after further review, reflecting systemic communication and procedural gaps(22).

Although justification is a medicolegal mandate, inconsistent application and workplace cultures that discourage autonomous critical assessment hinder its effectiveness(21). Encouraging radiographers to engage in critical thinking can lead to better justification practices, thereby enhancing patient safety by reducing unnecessary radiation exposure (21). The linear no-threshold (LNT) model supports the premise that any radiation dose carries some cancer risk, reinforcing the need for strict justification (23,24). Optimization also involves accurate and sufficient information on RRFs to guide dose management, including the use of diagnostic reference levels (DRLs) and adherence to regulations, such as the Ionizing Radiation (Medical Exposure) Regulations, particularly for vulnerable groups, such as pediatric patients.

Implementing digital or electronic radiology request form (RRF) systems presents a promising solution to address the widespread issues of incomplete and inaccurate form completion identified in this study. Electronic RRFs can include mandatory fields, standardized templates, and real-time validation checks to ensure that critical patient information such as allergy history, renal function, and last menstrual period is consistently provided. Additionally, digital systems facilitate improved communication and data sharing between referring clinicians and radiology departments, potentially enhancing the justification process and reducing unnecessary radiation exposure. The adoption of such technology, along with targeted training and protocol standardization, could significantly improve the quality and completeness of referral information, thereby bolstering diagnostic accuracy and patient safety.

The strengths of this study include its prospective, descriptive, cross-sectional design encompassing a large sample size (n = 1001) across five diverse healthcare institutions, thereby enhancing the generalizability of the results within Khartoum State. The use of a standardized data collection tool ensured the systematic extraction of RRF information, providing comprehensive insights into form completion rates and associated clinical variables. However, limitations include its focus on a single geographic region, which may limit its broader applicability. Additionally, reliance

on documented information without direct observation of clinical workflows may overlook contextual factors influencing form completion. The study also did not assess the direct clinical outcomes related to incomplete RRFs or the impact of interventions to improve form quality.

Future studies should investigate the implementation of electronic RRF systems and their effectiveness in enhancing data completeness and clinical communication, as indicated by this research. Examining the link between the completeness of RRFs and diagnostic accuracy or patient outcomes would offer valuable insights to shape policies and practices. Additionally, qualitative research into the obstacles and enablers of precise form completion by referring clinicians could inform targeted educational and systemic interventions.

Conclusion

This study successfully addressed the research problem by systematically evaluating the completeness and accuracy of radiology request forms (RRFs) for CT imaging across multiple hospitals in Khartoum State. The findings demonstrate that significant deficiencies persist in critical patient information, such as allergy history, renal function tests, and clinical history, which pose risks to diagnostic accuracy and patient safety. Although the study did not find that physician rank significantly influenced form quality, it highlighted systemic issues in form-filling practices and interdepartmental communication. Therefore, although the

research problem of incomplete and inaccurate RRFs remains unresolved, the study has effectively achieved its objectives by identifying specific gaps and providing a comprehensive assessment of current practices. These insights establish a foundation for targeted interventions, including standardized protocols, enhanced training, and improved collaboration, which are essential steps toward resolving the identified issues and optimizing CT diagnostic precision and patient safety.

List of Abbreviations

CIN	Contrast-Induced Nephropathy
CT	Computed tomography
FDA	Food and Drug Administration
LMP	last menstrual period
mSv	Millisieverts
RRFs	Radiography Request Forms
SPSS	Statistical Package for the Social Sciences
U.S.	United States

Conflict of Interest Declaration:

The authors declare no conflicts of interest in this manuscript.

Author Contributions:

MZ and TA contributed to the research design and implementation. AE, FA, and GH collected the data and wrote the initial draft. AE analyzed the results and wrote the manuscript. AE conceived and supervised the study.

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Disclosure of AI Usage

The authors used Paperpal to check the grammar, assist with the literature search, and perform plagiarism checks and citations during the preparation of this manuscript. After using this service, the authors reviewed and edited the content as needed and take full responsibility for the content of the published work.

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Liver functions alterations in preeclampsia: alanine aminotransferase & ALBI score as a marker of disease severity in a Sudanese cohort

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Abstract

Background: Preeclampsia is a multisystem hypertensive disorder of pregnancy characterized by endothelial dysfunction, systemic inflammation, and target organ injury, including hepatic involvement. Elevated liver enzymes, particularly alanine aminotransferase (ALT) and aspartate aminotransferase (AST), are frequently observed in severe disease and serve as biochemical markers of hepatocellular injury resulting from hepatic ischemia and endothelial dysfunction.

Objectives: This study aimed to assess the association between liver enzymes, ALBI score, and disease severity among Sudanese women with preeclampsia, and to evaluate the diagnostic performance of ALT and ALBI score for predicting severe preeclampsia.

Methods: This analytical cross-sectional study was conducted at Kosti Maternity Hospital, Sudan. Forty-five women with preeclampsia were enrolled and classified as mild or severe according to World Health Organization (WHO) and American College of Obstetricians and Gynecologists (ACOG) criteria. Clinical and laboratory parameters were assessed. The albumin–bilirubin (ALBI) score was calculated using the standard formula ($\log_{10} \text{bilirubin} \times 0.66 + \text{albumin} \times -0.085$), with bilirubin expressed in $\mu\text{mol/L}$ and albumin in g/L . Group comparisons and receiver operating characteristic (ROC) curve analysis were performed.

Results: ALT levels were significantly higher in severe preeclampsia compared with mild cases ($p = 0.035$), while no significant differences were observed for ALBI score ($p = 0.271$). ROC analysis showed that ALT had modest discriminatory ability ($\text{AUC} = 0.609$, $p = 0.025$), whereas ALBI score demonstrated limited performance ($\text{AUC} = 0.596$, $p = 0.268$).

Conclusions: ALT is significantly associated with severe preeclampsia and may serve as a useful adjunctive marker for identifying women at higher risk of complications. The ALBI score did not show a significant association with disease severity. Further validation in larger, multicenter studies is warranted.

Keywords: Preeclampsia; Liver enzymes; Alanine aminotransferase; Albumin–bilirubin score; Disease severity; Sudan

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Introduction

Preeclampsia is a pregnancy-specific hypertensive disorder that affects approximately 2–8% of pregnancies worldwide and remains a leading cause of maternal and perinatal morbidity and mortality, particularly in low- and middle-income countries [1,2]. It is characterized by new-onset hypertension after 20 weeks of gestation accompanied by proteinuria or maternal organ dysfunction [1]. Despite advances in obstetric care, the pathophysiology of preeclampsia is not completely understood; however, abnormal placentation, endothelial dysfunction, immune dysregulation, and systemic inflammation are central mechanisms [2,3].

Hepatic involvement is a well-recognized manifestation of severe preeclampsia. Liver injury may result from microvascular endothelial damage, fibrin deposition, and hepatic ischemia, leading to elevated transaminases and, in severe cases, hemolysis, elevated liver enzymes, and low platelets (HELLP) syndrome [4]. Elevation of alanine aminotransferase (ALT) and aspartate aminotransferase (AST) reflects hepatocellular injury and has been incorporated into the diagnostic criteria for severe disease [1,4].

Serum albumin levels are frequently reduced in preeclampsia due to increased vascular permeability and proteinuria, contributing to

edema and altered oncotic pressure [5]. The albumin–bilirubin (ALBI) score, originally developed as a prognostic tool in chronic liver disease, integrates serum albumin and bilirubin into a composite index reflecting liver functional reserve [6]. Although widely studied in hepatology, its potential role in obstetric disorders such as preeclampsia remains insufficiently explored.

In resource-limited settings such as Sudan, access to advanced biomarkers may be restricted. Therefore, identifying reliable, inexpensive, and routinely available laboratory markers to predict disease severity is of substantial clinical importance. Few studies from sub-Saharan Africa have evaluated the relationship between liver function parameters and preeclampsia severity.

Accordingly, this study aimed to assess the association between liver enzymes, serum albumin, bilirubin, and ALBI score with the severity of preeclampsia among women attending a tertiary maternity hospital in Sudan.

Materials and Methods

Study design and setting

This analytical cross-sectional study was conducted at Kosti Maternity Hospital, White Nile State, Sudan, between September and December 2022. Kosti Maternity Hospital is

a governmental tertiary care center affiliated with the Ministry of Health and provides comprehensive obstetric and gynecological services. The study was reported in accordance with the STROBE guidelines for cross-sectional studies.

Study population

Pregnant women diagnosed with preeclampsia during the study period were eligible for inclusion. Preeclampsia was defined as new-onset hypertension (systolic blood pressure ≥ 140 mmHg and/or diastolic blood pressure ≥ 90 mmHg on at least two occasions at least 6 hours apart) occurring after 20 weeks of gestation, accompanied by proteinuria (≥ 300 mg/24 hours) or evidence of maternal organ dysfunction [1].

Participants were classified into mild and severe preeclampsia according to WHO and ACOG criteria [1,7]. Severe preeclampsia was diagnosed in the presence of one or more of the following: systolic blood pressure ≥ 160 mmHg or diastolic blood pressure ≥ 110 mmHg, severe proteinuria (≥ 5 g/24 hours), thrombocytopenia, renal insufficiency, hepatic dysfunction (elevated liver enzymes to twice normal concentration), pulmonary edema, neurological symptoms, or HELLP syndrome.

Inclusion and exclusion criteria

Women diagnosed with preeclampsia who agreed to participate and provided written informed consent were included.

Exclusion criteria included pre-existing chronic liver disease, diabetes mellitus, chronic kidney disease, autoimmune disorders, tuberculosis, cardiovascular disease, bone marrow disorders, myeloproliferative diseases, or any condition that could confound inflammatory or biochemical parameters.

Sampling method

A total coverage sampling approach was used, including all eligible preeclamptic women presenting during the study period. Forty-five participants were enrolled.

Data collection

Data were collected using a semi-structured questionnaire after obtaining written informed consent. Information included maternal age, parity, gestational age, clinical presentation (headache, visual disturbances, epigastric pain, jaundice, lower limb edema), and relevant obstetric and medical history.

Blood pressure was measured using a calibrated sphygmomanometer according to standard procedures. Midstream urine samples were collected for semi-quantitative proteinuria assessment using dipstick testing.

Laboratory investigations

Five milliliters of venous blood were collected under aseptic conditions. Samples were divided into EDTA tubes for hematological analysis and lithium heparin tubes for biochemical assays.

Complete blood count was analyzed using an automated hematology analyzer (Sysmex KX-21N, Japan). Biochemical parameters including serum ALT, AST, alkaline phosphatase (ALP), total bilirubin, total protein, albumin, and creatinine were measured using a fully automated chemistry analyzer (Mindray BS-200, China).

The albumin–bilirubin (ALBI) score was calculated using the formula:

ALBI score = (log₁₀ bilirubin × 0.66) + (albumin × –0.085) where bilirubin is expressed in µmol/L and albumin in g/L [6]. Bilirubin values expressed in mg/dL were converted to µmol/L prior to ALBI calculation.

Statistical analysis

Data were analyzed using SPSS version 25. Continuous variables were tested for normality and presented as mean ± standard deviation or median (interquartile range) as appropriate. Categorical variables were expressed as frequencies and percentages.

Comparisons between mild and severe preeclampsia were performed using Student's t-test or Mann–Whitney U test for continuous variables and chi-square or Fisher's exact test for categorical variables. Receiver operating characteristic (ROC) curve analysis was performed to evaluate the diagnostic performance of ALT and ALBI score in predicting severe preeclampsia. The area under the curve (AUC), sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated. A p value <0.05 was considered statistically significant. A multivariable logistic regression analysis was performed to identify independent predictors of severe preeclampsia. Variables with p < 0.20 in univariable analysis or those clinically relevant were included in the model. Adjusted odds ratios (AORs) with 95% confidence intervals were reported.

Ethics consideration

The study was conducted in accordance with the Declaration of Helsinki. Ethical approval was obtained from Kosti Maternity Hospital, and the study was also approved by the Institutional Ethical Committee of the Faculty of Medicine, The National Ribat University, Sudan (Approval Number NRU-MED-DRC 91082022, 10/8/2022). Written informed consent was obtained from all participants prior to enrollment.

Results

Study population

A total of 45 pregnant women diagnosed with preeclampsia were included in the study. According to the World Health Organization and American College of Obstetricians and Gynecologists criteria, 23 women (51.1%) were classified as having mild preeclampsia and 22 (48.9%) as having severe preeclampsia.

Baseline demographic and obstetric characteristics

The median age of participants was 26 years (IQR 21–29). The median parity was 1 (IQR 0–2), and the mean gestational age at presentation was 34.38 ± 2.47 weeks.

There were no statistically significant differences between women with mild and severe preeclampsia regarding age (p = 0.632), parity (p = 0.142), or gestational age (p = 0.084).

As expected based on the diagnostic classification criteria, systolic and diastolic blood pressure values were higher in the severe preeclampsia group. These variables are presented descriptively without inferential statistical comparison.

Clinical presentation

Headache was significantly more common among women with severe preeclampsia (95.5%) compared with those with mild disease (65.2%) (p = 0.022). Upper abdominal pain occurred in 36.4% of severe cases versus 8.7% of mild cases (p = 0.035), while jaundice was observed exclusively in the severe group (18.2%) (p = 0.049).

Visual disturbances were reported only in severe cases (13.6%), although the difference did not reach statistical significance (p = 0.109). Lower limb swelling, multiple gestations, history of hypertension, previous preeclampsia, family history of preeclampsia, and degree of proteinuria were comparable between groups (all p > 0.05) (Table 2).

Liver function tests and biochemical parameters

Serum protein profile demonstrated a median total protein of 7.0 g/dL (IQR: 6.2–7.2) and median albumin of 3.50 g/dL (IQR: 3.10–4.00).

The ALBI score had a median of -0.38 (IQR: -0.48 to -0.29).

The overall median ALT was 29.0 U/L (IQR 17.0–40.0), and median AST was 37.0 U/L (IQR 30.0–50.0). Mean ALP was 113.76 ± 45.93 U/L. Median total bilirubin and albumin were 0.70 mg/dL (IQR 0.60–0.90) and 3.50 g/dL (IQR 3.10–4.00), respectively.

ALT levels were significantly higher in women with severe preeclampsia compared with those with mild disease ($p = 0.035$). No statistically significant differences were observed between groups in AST ($p = 0.964$), ALP ($p = 0.141$), total bilirubin ($p = 0.713$), total protein ($p = 0.198$), albumin ($p = 0.085$), or ALBI score ($p = 0.271$) (Table 3).

Diagnostic performance of liver-related indices

Receiver operating characteristic (ROC) curve analysis demonstrated that ALT had a modest ability to discriminate severe from mild preeclampsia, with an area under the curve (AUC) of 0.609 ($p = 0.025$). An ALT cutoff value >45 U/L yielded a sensitivity of 45.5% and specificity of 100%, with a positive predictive value of 100% and a negative predictive value of 65.7%.

The ALBI score showed limited discriminatory performance (AUC = 0.596, $p = 0.268$). A cutoff value > -0.46 provided a sensitivity of 81.8% but low specificity (39.1%). **Table 4**

In multivariable logistic regression analysis, ALT remained an independent predictor of severe preeclampsia, while ALBI score was not significantly associated with disease severity.

Discussion

In this analytical cross-sectional study of Sudanese women with preeclampsia, we evaluated the association between liver enzymes, serum albumin, bilirubin, and ALBI score with disease severity. The principal findings were that alanine aminotransferase (ALT) levels were significantly higher in severe preeclampsia compared with mild disease, and ALT demonstrated modest discriminatory ability for identifying severe cases. In contrast, AST, ALP, bilirubin, albumin, and ALBI score were not significantly associated with severity.

The rationale for evaluating the albumin–bilirubin (ALBI) score in preeclampsia is based on its ability to integrate two clinically relevant parameters reflecting hepatic function and systemic disease processes. Serum albumin reflects nutritional status, systemic inflammation, and endothelial dysfunction, while bilirubin may indicate hepatic excretory function and, in some cases, hemolysis. Given that preeclampsia is characterized by endothelial injury, capillary leakage, and potential hepatic involvement, the ALBI score may theoretically provide a composite measure of disease severity. However, its utility in obstetric populations remains insufficiently validated.

Hepatic involvement represents a key manifestation of severe preeclampsia and ranges from mild transaminase elevation to HELLP syndrome and, rarely, hepatic rupture

[4]. The underlying mechanism involves hepatic sinusoidal endothelial damage, fibrin deposition, and ischemia, leading to hepatocellular injury and subsequent elevation of transaminases [3,4]. These findings support the role of endothelial dysfunction and hepatic ischemia in the pathophysiology of severe disease.

Our finding that ALT levels were significantly higher in severe preeclampsia is consistent with current diagnostic frameworks. According to the American College of Obstetricians and Gynecologists, elevated liver enzymes to twice the normal concentration are considered a criterion for severe disease [1]. ALT is more liver-specific than AST and may better reflect hepatocellular injury in the absence of significant hemolysis or muscle involvement. Importantly, in multivariable analysis, ALT remained independently associated with severe preeclampsia after adjustment for potential confounders, further supporting its clinical relevance as a marker of disease severity.

In contrast, AST did not differ significantly between mild and severe groups in our study. Although AST elevation is frequently reported in severe preeclampsia and HELLP syndrome [4], it is less specific for liver injury and may be influenced by hemolysis and other systemic factors. The lack of statistical significance in this study may reflect limited statistical power due to the relatively small sample size and the absence of advanced

hepatic complications in the study population.

Serum albumin levels were lower in severe cases, although the difference did not reach statistical significance. Hypoalbuminemia in preeclampsia is attributed to increased capillary permeability, systemic inflammation, and urinary protein loss [5]. While albumin alone was not independently associated with disease severity in this study, it remains an important indicator of endothelial dysfunction and disease burden.

The ALBI score, originally developed to assess liver functional reserve in chronic liver disease [6], integrates serum albumin and bilirubin into a composite index. In the present study, ALBI score showed limited ability to discriminate between mild and severe preeclampsia. Although sensitivity was relatively high at the selected cutoff, specificity was low, limiting its clinical utility as a standalone predictor. This may be explained by the relatively normal bilirubin levels observed in both groups, indicating that significant cholestatic or hemolytic processes were uncommon in this cohort.

Receiver operating characteristic analysis demonstrated that ALT had modest discriminatory power (AUC 0.609) but excellent specificity (100%) at a cutoff >45 U/L. High specificity suggests that markedly elevated ALT may reliably identify women at higher risk of severe disease. However, the relatively low sensitivity indicates that

normal ALT levels do not exclude severe preeclampsia. Therefore, ALT should be interpreted within a broader clinical and laboratory context rather than used in isolation.

From a clinical perspective, these findings are particularly relevant in resource-limited settings such as Sudan, where access to advanced biomarkers may be restricted. Routine liver function tests are inexpensive and widely available. Identifying simple laboratory markers associated with disease severity may support risk stratification and timely referral to higher levels of care.

The absence of significant differences in bilirubin and ALP between groups may reflect the spectrum of disease severity in this cohort. Most participants presented without advanced hepatic complications, and cases of overt HELLP syndrome were uncommon. This suggests that transaminase elevation may occur earlier in the disease process and could serve as a more sensitive indicator of hepatic involvement.

Overall, these findings reinforce the concept that hepatic dysfunction in preeclampsia is part of a broader systemic process characterized by endothelial injury and inflammation [2,3]. While composite indices such as ALBI are conceptually attractive due to their simplicity, further validation in larger obstetric cohorts is required before routine clinical application.

Recent observational studies have highlighted the role of hepatic biomarkers in stratifying disease severity in hypertensive disorders of pregnancy. A prospective cohort study by Breetveld et al. demonstrated that elevated transaminases were independently associated with adverse maternal outcomes in severe preeclampsia, even in the absence of HELLP syndrome [8]. Similarly, Kamel et al. reported a positive correlation between ALT levels and markers of endothelial dysfunction and systemic inflammation [9], supporting the concept that hepatocellular injury reflects widespread microvascular compromise. These findings are consistent with our results.

In contrast, studies evaluating composite indices incorporating albumin and bilirubin have reported inconsistent findings. A multicenter study by Zhang et al. found no significant independent association between ALBI score and disease severity after multivariable adjustment [10]. Similarly, El-Sayed et al. reported limited discriminatory performance of ALBI in predicting severe maternal outcomes, attributed to relatively preserved bilirubin levels in most patients [11]. These findings align with our results and suggest that the utility of ALBI in preeclampsia may be limited.

Strengths and Limitations

This study has several strengths. First, it addresses an underexplored area in sub-Saharan Africa by evaluating the association between liver-related biochemical parameters

and preeclampsia severity. Second, all laboratory parameters assessed are routinely available and cost-effective, enhancing the translational applicability of the findings in low-resource settings. Third, standardized diagnostic criteria from the American College of Obstetricians and Gynecologists and the World Health Organization were used to classify disease severity, ensuring consistency and comparability [1,2]. Finally, ROC curve analysis was applied to evaluate the diagnostic performance of ALT and ALBI score, providing clinically meaningful performance metrics. Several limitations should be acknowledged. First, the analytical cross-sectional design precludes causal inference and limits the ability to assess temporal relationships between liver function parameters and disease progression. Second, the relatively small sample size may have reduced the statistical power to detect significant associations, particularly for variables such as AST, albumin, and ALBI score. Third, the study was conducted at a single center, which may limit the generalizability of the findings to other populations and healthcare settings. Fourth, although several clinical and biochemical variables were assessed, residual confounding cannot be excluded, particularly in the absence of comprehensive multivariable adjustment for all potential predictors. Fifth, the absence of longitudinal follow-up prevented evaluation of maternal and perinatal outcomes. Finally, advanced biomarkers, including angiogenic and

inflammatory markers, were not measured, limiting comparison with emerging predictors of preeclampsia severity.

Conclusion

In this cross-sectional study of Sudanese women with preeclampsia, elevated ALT was significantly associated with severe disease and demonstrated high specificity for identifying severe cases. Other liver-related parameters, including AST, bilirubin, albumin, and ALBI score, were not independently associated with severity, and ALBI showed limited discriminatory ability.

Routine assessment of liver enzymes, particularly ALT, may provide clinically useful information for risk stratification in preeclampsia, especially in resource-limited settings. Larger prospective studies are needed to confirm these findings and to further define the role of composite liver indices in the management of hypertensive disorders of pregnancy.

Competing interests

The authors have no relevant financial or non-financial interest to disclose. The authors declare that they have no competing interests.

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Table (1): Comparison between cases with mild and severe preeclampsia regarding baseline demographic characteristics

Baseline demographic characteristics		All preeclampsia patients (N= 45)	Mild preeclampsia (N= 23)	Severe preeclampsia (N= 22)	Test value	P-value
Age (years)	Median (IQR)	26 (21 - 29)	26.0 (20.0–33.0)	24.0 (21.0–27.0)	$z_{MWU}=0.479$	0.632
Parity	Median (IQR)	1 (0 - 2)	0.0 (0.0–2.0)	1.0 (0.0–3.0)	$z_{MWU}=1.470$	0.142
Gestational age (weeks)	Mean±SD	34.38± 2.47	35.0 ± 2.35	33.7 ± 2.5	T=1.769	0.084
SBP (mm/Hg)	Median (IQR)	150 (140-160)	150 (140–160)	160 (150–180)	-	-
DBP (mm/Hg)	Median (IQR)	100 (100-110)	100 (90–100)	110 (110–130)	-	-

P value >0.05: Not significant, *P value <0.05 is significant, **p<0.01 is highly significant.
T: Student T test, ZMWU: Mann-Whitney U test, X²: Chi-Square Test
SD: standard deviation, IQR: Interquartile range, SBP: Systolic blood pressure, DBP: Diastolic blood pressure

Table (2): Comparison between cases with mild and severe preeclampsia regarding baseline clinical characteristics

		Mild preeclampsia (N= 23)		Severe preeclampsia (N= 22)		Chi-Square Test	
		N	%	N	%	X ²	p-value
Headache	Yes	15	65.2%	21	95.5%	6.425	0.022 *FET
	No	8	34.8%	1	4.5%		
Visual disturbance	Yes	0	0.0%	3	13.6%	3.360	0.109 ^{FET}
	No	23	100.0%	19	86.4%		
Upper abdominal pain	Yes	2	8.7%	8	36.4%	4.980	0.035 *FET
	No	21	91.3%	14	63.6%		
Jaundice	Yes	0	0.0%	4	18.2%	4.590	0.049 *FET
	No	23	100.0%	18	81.8%		
Lower limb swelling	Yes	13	56.5%	11	50.0%	0.192	0.661
	No	10	43.5%	11	50.0%		
Multiple gestations	Yes	2	8.7%	3	13.6%	0.278	0.665 ^{FET}
	No	21	91.3%	19	86.4%		
Hypertension	Yes	1	4.3%	4	18.2%	2.179	0.187 ^{FET}
	No	22	95.7%	18	81.8%		
Previous preeclampsia	Yes	0	0.0%	1	4.5%	1.069	0.489 ^{FET}
	No	23	100.0%	21	95.5%		
Hematological disorder	Yes	0	0.0%	0	0.0%	-	-
	No	23	100.0%	22	100.0%		
Family history of preeclampsia	Yes	10	43.5%	5	22.7%	2.179	0.140
	No	13	56.5%	17	77.3%		
Proteinuria	+	9	39.1%	4	18.2%	2.435	0.353 ^{MC}
	2+	12	52.2%	15	68.2%		
	3+	2	8.7%	3	13.6%		

P value >0.05: Not significant, *P value <0.05 is significant, **p<0.01 is highly significant.

FET: Fischer Exact test, MC: Monte-Carlo correction

Table (3): Liver functions test and biochemical parameters

		All preeclampsia patients (N= 45)	Mild preeclampsia (N= 23)	Severe preeclampsia (N= 22)	Test value	P-value
ALP (U/L)	Mean ± SD	113.76 ± 45.93	109.39 ± 42.81	118.3 ± 49.6	T= 0.647	0.141
AST (U/L)	Median (IQR)	37.0 (30.0–50.0)	37.0 (30.0–47.0)	35.0 (29.0–71.9)	Z _{MWU} = 0.045	0.964
ALT (U/L)	Median (IQR)	29.0 (17.0–40.0)	28.0 (19.0–32.0)	35.5 (15.0–52.0)	Z _{MWU} = 2.099	0.035*
Total protein (g/dL)	Median (IQR)	7.0 (6.2–7.2)	7.1 (6.4–7.5)	6.7 (6.0–7.2)	Z _{MWU} = 1.288	0.198
Albumin (g/dL)	Median (IQR)	3.50 (3.10–4.00)	3.9 (3.2–4.1)	3.3 (3.1–3.9)	Z _{MWU} = 1.723	0.085
Total bilirubin (mg/dL)	Median (IQR)	0.70 (0.60–0.90)	0.7 (0.4–0.9)	0.8 (0.6–0.9)	Z _{MWU} = 0.368	0.713
ALBI	Median (IQR)	-0.38 (-0.48– -0.29)	-0.41 (-0.55– -0.29)	-0.38 (-0.44– -0.26)	Z _{MWU} = 1.102	0.271

P value >0.05: Not significant, *P value <0.05 is significant, **p<0.01 is highly significant.

T: Student T test, ZMWU: Mann-Whitney U test.

Table 4: Validity of novel indices in in predicting severe preeclampsia.

	Best cut off value	AUC	Sensitivity	Specificity	PPV	NPV	P-value
ALT	>45.0	0.609	45.5%	100%	100%	65.7%	0.025
ALBI	> -0.46	0.596	81.8%	39.1%	56.2%	69.2%	0.268

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Sociodemographic Characteristics, Pattern, and Risk Factors Among Breast Cancer Women Patients in Yemen

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Abstract

Breast cancer is the most prevalent malignancy among women globally. Sociodemographic characteristics play a critical role in breast cancer because they heavily influence screening access, stage at diagnosis, and treatment adherence. This study aimed to investigate the pattern of general and sociodemographic characteristics and risk factors among women patients at the National Cancer Control Foundation (NCCF) and National Oncology Center (NOC), Yemen. This prospective, multi-center, cross-sectional study was conducted at national oncology centers in Yemen over a period of 12 months. Data were collected from patients' medical records and by interviewing patients on admission, during follow-up, and on discharge. Of 450 patients enrolled, breast cancer was more prevalent among women younger than 50 years, with the highest proportion in the 40-49 year age group (28%), and among married women (77.3%). A minority of participants had a family history (11.1%) or previous personal history (7.3%) of breast cancer. The majority of patients had age at menarche ≥ 12 years (87.6%). Social status, age at menarche, smoking history, khat-leaf chewing history, and smokeless tobacco (shammah) use history were characteristics significantly associated with histopathologic type of breast cancer. This study population had distinctive general and sociodemographic features that likely contribute to patterns of late diagnosis and underscore the need for targeted screening strategies among Yemeni women.

Keywords: Sociodemographic characteristics; risk factors; breast cancer; Yemen

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Introduction

Breast cancer is the most prevalent malignancy among women globally, accounting for a significant proportion of female cancer cases and cancer-related deaths in nearly 90% of countries. It is the second leading cause of all cancer-related deaths and the leading cause of cancer mortality in women, with higher mortality rates in low-income countries due to late-stage diagnosis and limited access to life-saving treatment, and higher incidence rates particularly among younger women in certain regions.^{1,2} According to 2022 data, breast cancer was the most commonly diagnosed cancer in Yemen, with approximately 2,872 new female cancer cases (31.1%), and the leading cause of cancer death among Yemeni women.³

Sociodemographic factors such as age, income, educational attainment, occupation, marital status, geographic residence (urban versus rural), and ethnic or religious affiliation significantly affect breast cancer risk, clinical presentation (stage at diagnosis), and treatment outcomes. These factors frequently interact with lifestyle and reproductive variables; however, observed patterns vary considerably worldwide. In some regions, higher socioeconomic status (SES) is occasionally associated with elevated risk, whereas in others, lower SES or educational level is correlated with diagnosis at a more advanced stage.⁴

The epidemiological literature indicates that diagnosis of breast cancer at advanced stages is significantly correlated with sociodemographic factors including age, religion, educational level, occupation,

marital status, dietary habits, family size, monthly income, unemployment status, and family history of breast cancer.^{5,6} Physical activity and tobacco use are modifiable risk factors linked to breast cancer incidence to varying extents.^{7,8} Several studies have demonstrated that breast cancer is associated with characteristics of women's reproductive life, including early menarche, nulliparity, low parity or advanced maternal age at first childbirth, history of breastfeeding, delayed menopause, and hormonal effects (endogenous and exogenous).⁹⁻¹²

Data from Arab countries on breast cancer vary by region. Political instability, military conflict, and poor planning have kept many Arab populations from benefiting fully from the medical advances of the past several decades.¹³ A study on the burden of breast cancer in the Arab world found that its incidence among Arab women has increased over the past three decades.¹⁴ The World Health Organization has reported that although more than 60,000 cancer patients in Yemen have received cancer treatment, an estimated 30,000 remain in urgent need of active treatment.¹⁵

This study is motivated by the increasing number of newly diagnosed breast cancer cases reported annually by national cancer registries in Yemen, together with a lack of clinical studies on the sociodemographic characteristics of breast cancer in Yemen and their association with disease risk. These gaps highlight the need for research focused on Yemeni female patients.

Yemen needs to strengthen its regional and national cancer registries to determine the

national cancer burden as a first step toward a comprehensive cancer control strategy, and there is an urgent need to initiate early breast cancer screening given its high prevalence among Yemeni women. This study aimed to investigate the pattern of sociodemographic characteristics, past and current medical history, family and personal history, menstrual history, hormonal use history, and risk factors for breast cancer, and to examine the association of these variables with diagnosed histopathologic type of breast cancer among Yemeni women diagnosed at national oncology centers.

Subjects and Methods

A prospective, multi-center, cross-sectional study was conducted at the National Cancer Control Foundation (NCCF) and the National Oncology Center (NOC), Yemen. All female patients with confirmed breast cancer admitted to NCCF and NOC during a 12-month period, who had complete medical records and regular treatment and follow-up schedules, were included. Exclusion criteria comprised male patients with breast cancer, women with benign breast lumps, and women who did not complete treatment.

Based on the cancer statistics of national registries in Yemen and the Research Advisors sample size calculator (2006)¹⁶ using the Krejcie and Morgan formula, the required sample size was approximately 346 cases (assuming a total annual population of 3,000 cases at national oncology centers), at a 95% confidence level and 5% margin of error. The actual sample size was 450 cases; this increase was intended to compensate for potential attrition due to patients dropping out

or becoming unreachable, and was intended to yield statistically reliable and generalizable results.

Data were collected using a pretested, structured data collection sheet, drawn from patients' medical records and through interviews conducted on admission, during follow-up, and at discharge. The data collection form was organized into seven sections. A database was created in Microsoft Excel 2016 and analyzed using SPSS version 23. The chi-square test was used to investigate associations between diagnosed histopathologic type of breast cancer and selected characteristic variables, with statistical significance set at $p \leq 0.05$.

This study was conducted in accordance with the principles of the Declaration of Helsinki. Ethical approval was granted by the Ethics Committee of The National Ribat University, Khartoum, Sudan, on 18 Septemberth 2019 (approval reference Ph.D/Pharm/2019/no:2). Formal approval to conduct the research on the study sample was also obtained from the institutional review board of the national oncology centers in Yemen. Informed consent was obtained from all enrolled patients; a detailed explanation of the study was provided before data collection, confidentiality was ensured, and patients were informed that the information collected was for research purposes only and that participation was entirely voluntary.

Results:

Characteristics of the Study Population

Sociodemographic Characteristics of Participants

A total of 450 female patients with breast cancer were enrolled. Mean age $\pm$ SD was 49.30 ± 12.55 years. The highest proportion of participants were aged 40-49 years (28%), married (77.3%), resident in rural areas (52.2%), and unemployed, mostly housewives (67.8%) as shown in **Table 1**.

Past and Current Medical History

Most participants had comorbidities (74.7%). Hypertension was the most prevalent comorbidity (31.1%), followed by diabetes mellitus (15.9%).

Family History of Cancer

A minority of participants had a family history of breast cancer (11.1%), ovarian cancer (2.4%), or prostate cancer (1.1%).

Personal History of Breast Cancer and Previous Breast Surgery

A small proportion of participants had a personal history of breast cancer (7.3%). Among these, the majority (69.6%) had undergone lumpectomy as their initial breast-conserving surgery, compared with 15.2% who underwent simple mastectomy and 15.2% who underwent modified radical mastectomy (MRM).

Menstrual History

A minority of patients (12.4%) had age at menarche before 12 years. Slightly more than half of patients (51.6%) were postmenopausal; nearly one-third of these (35.8%) experienced menopause between 50 and 54 years of age, and most (94.4%) experienced natural menopause.

Hormonal and Reproductive History

Most patients were non-users of contraception (61.8%), had parity (86.7%),

had 1-5 pregnancies (72.6%), and had their first pregnancy after age 15 (90%).

Risk Factors for Breast Cancer

Most participants reported physical inactivity and a sedentary lifestyle (74.2%), had no history of chest radiation exposure (79.6%), were non-smokers (59.6%), chewed *khat* (*Catha edulis*) leaves (65.6%), and did not use smokeless tobacco (shammah) (90.7%) (see **Table 2**).

Association Between Histopathologic Type and Participant Characteristics

There was a statistically significant association between diagnosed histopathologic type of breast cancer and marital status ($p = 0.002$), age at menarche ($p = 0.045$), smoking history ($p = 0.009$), khat chewing history ($p = 0.008$), and smokeless tobacco (shammah) use history ($p = 0.048$).

Discussion

The higher incidence of breast cancer among Yemeni women aged 40-49 years in this study is likely attributable to several factors, including the generally higher incidence among younger women in developing countries such as Yemen compared with developed Western countries, together with low socioeconomic status, low educational level, and limited health awareness regarding early screening, leading to diagnosis at a more advanced stage within this age group. This finding is consistent with local and global studies reporting that most participants were aged 40-50 years.¹⁸⁻²⁰ In contrast, a recent local study²¹ found that most patients were aged 18-31 years, while another regional study²² found that most participants were aged ≥ 50 years.

Breast cancer is more prevalent among married women, particularly older, postmenopausal women, both locally and globally. Married women may face particular risk from lifestyle behaviors, environmental factors, hormonal factors, delayed childbearing, limited screening uptake, late-stage diagnosis, and traditional cultural norms. This finding is consistent with cultural patterns in Yemen and many Arab and Asian countries, where marriage is prevalent among adult women with breast cancer.^{17,19,23} In contrast, an Asian study²⁴ found a higher incidence of breast cancer among unmarried women, particularly lifelong single women, than among married women. Other studies similarly reported an association between marital status and breast cancer incidence.^{25,26} The distribution of breast cancer patients across urban and rural areas varies locally and globally. The perception that most Yemeni patients are rural residents may stem from more limited access to healthcare facilities, reliance on under-resourced rural clinics, lower socioeconomic status, and reduced awareness of breast cancer. Consistent with our findings, some studies found that most participants resided in rural areas.^{17,22,27} In contrast, other studies found higher proportions living in urban areas.^{21,23} Most breast cancer patients in this study were unemployed or housewives, potentially reflecting lower socioeconomic status, lower educational level, cultural norms, and traditional lifestyle patterns, particularly in rural areas. Consistent with our results, most patients were unemployed housewives in several studies^{22,27,28}, although other studies

reported that most patients were employed.^{17,29}

Women with breast cancer frequently have multiple chronic comorbidities, particularly cardiovascular, metabolic, and musculoskeletal conditions, alongside fatigue, insomnia, anorexia, and pain, which may contribute to psychological distress and affect survival, treatment tolerance, and quality of life. Consistent with our findings, global studies have found that hypertension, ischemic heart disease, heart failure, diabetes, and hyperlipidemia are highly prevalent among breast cancer patients and often increase after diagnosis.³⁰⁻³² In contrast, other studies³³⁻³⁶ found no comorbidities among their patients.

Family history of breast cancer is strongly relevant and significantly increases risk, suggesting genetic predisposition. First-degree family history has been associated with increased risk of estrogen receptor-positive (ER+), HER2-negative breast cancer and triple-negative breast cancer (TNBC).³⁷ Consistent with our findings, minor proportions of patients with family history of breast cancer have been reported elsewhere.^{34,38} In contrast, one study³⁹ found no patients with family history of breast cancer, whereas another study⁴⁰ reported that most patients had a family history.

A personal history of breast cancer significantly increases the risk of recurrence and requires enhanced, personalized surveillance, often involving annual mammography, potentially MRI, clinical examination, and sometimes genetic counseling. Previous breast surgery

(lumpectomy or mastectomy) and treatment (radiotherapy or chemotherapy) influence ongoing risk and the intensity of follow-up care for recurrence or new primary tumors. Consistent with our findings, small proportions of patients with personal history of breast cancer have been reported.^{21,36,40} A European study similarly found lumpectomy to be the most common primary surgery, whereas a Turkish study²³ found that most patients underwent total mastectomy.

Regarding age at menarche, global studies have found a significant relationship between early menarche (≤ 12 years) and breast cancer diagnosis, consistent with our findings.^{41,42} Postmenopausal status is generally more prevalent among breast cancer patients overall, with higher incidence globally; however, premenopausal breast cancer represents a greater relative burden in developing countries and often has distinct biological characteristics and poorer outcomes. Consistent with our findings, other studies have reported a majority of postmenopausal patients at diagnosis.⁴³⁻⁴⁵ Asian and African studies found higher proportions of premenopausal patients among Chinese and Nigerian women.^{46,47}

Consistent with the literature, age at menopause among postmenopausal patients in this study generally fell within the typical range of 45-55 years; later menopause (>55 years) is associated with increased breast cancer risk, reflecting prolonged estrogen exposure, while earlier menopause (<44 years) is associated with a protective effect and lower risk.^{45,48,49}

Regarding risk factors, some studies disagreed with our findings, reporting that most of their breast cancer cases had a history of physical activity^{27,28}, or chest radiation exposure.^{50,51} Smoking increases breast cancer risk, particularly when initiated at a younger age or continued for longer durations (>10 years, or >40 cigarettes/day).⁵² Consistent with our findings, several studies found that most patients were non-smokers.^{33,35,45,53} A correlation between smoking status and clinicopathological features of breast cancer has also been confirmed.^{53,54} Smoking is associated with a more severe immunohistochemical profile in younger smokers and with greater disease severity and higher mortality.⁵⁴

Higher prevalence of khat chewing, particularly among smokers, has been reported in Yemen, consistent with our findings.⁵⁵ In contrast, one local study²⁷ found that more than half of participants had never chewed khat. There is concern that heavy pesticide use in khat cultivation may contribute to cancer risk among habitual users, complicating interpretation of its health effects.⁵⁶ However, no studies have proven a direct correlation between khat chewing and breast cancer risk. In contrast to our findings, a Chinese study⁵⁷ investigating potential protective effects of khat confirmed a cytotoxic effect of khat extracts on human breast cancer cells, suggesting no positive association between khat chewing and breast cancer.

Higher proportions of patients with no exposure to smokeless tobacco have been documented elsewhere, consistent with our

findings.^{58,59} In contrast, another study found that most participants had a history of smokeless tobacco exposure.⁶⁰ Supporting our findings, an increased risk of breast cancer has been observed among women who ever used chewing tobacco^{58,60}, although another study found no statistically significant association between smokeless tobacco exposure and breast cancer.⁵⁹

Strengths of this study include its assessment of culturally specific risk factors (khat and shammah use), multi-center design, and relatively large sample size, which enhance generalizability and reduce institutional bias. Limitations include the cross-sectional design, which is susceptible to bias and precludes causal inference, difficulties in data collection due to incomplete medical files, registries to determine breast cancer prevalence and to initiate early screening programs and awareness strategies; Yemeni women older than 40 years are recommended to undergo mammography at least once a year.

Declaration of Interest

There is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

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Author Contributions

The first draft of the manuscript was written by all authors, and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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challenges communicating with some patients, and limited financial support.

Conclusion

This study population had distinctive general and sociodemographic characteristics. Breast cancer was more prevalent among middle-aged women (40-50 years), married women, rural residents, and housewives, which may reflect cultural norms and concerns contributing to late detection and diagnosis among Yemeni women. Marital status, age at menarche, smoking history, khat chewing history, and smokeless tobacco (shammah) use history were characteristics significantly associated with histopathologic type of breast cancer. These findings highlight the need to develop national cancer

Table (1): Distribution of frequency and percentage of sociodemographic characteristics of participants

Sociodemographic characteristics variables	Frequency (n)	Percentage (%)
Age group		
20-39 years old	97	21.6
40-49 years old	126	28
50-59 years old	113	25.1
60-69 years old	80	17.8
≥70 years old	34	7.6
Total	450	100
Social status		
Married	348	77.3
Single	30	6.7
Divorced	19	4.2
Widowed	53	11.8
Total	450	100
Place of residence		
Urban areas	215	47.8
Rural areas	235	52.2
Total	450	100
Patient's employment status		
Employed	145	32.2
Unemployed	305	67.8
Total	450	100

Table (2): Distribution of frequency and percentage of risk factors of breast cancer

Variable	Frequency (n)	Percentage (%)
Physical activity		
Yes	116	25.8
No	334	74.2
Total	450	100
Exposure to chest radiation		
Yes	92	20.4
No	358	79.6
Total	450	100
Smoking cigarettes or Shisha		
Yes	182	40.4
No	268	59.6
Total	450	100
khat (Catha edulis) (Khat) leaves chewing		
Yes	295	65.6
No	155	34.4
Total	450	100
Smokeless tobacco/Shammah taking		
Yes	42	9.3
No	408	90.7
Total	450	100

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Surgical Impact on Women amid El Fasher City Siege Warfare (April 2024–October 2025)

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Abstract

Background: El Fasher, the capital of North Darfur State, underwent a brutal 18-month siege beginning in April 2024, ending with the city's capture by the Rapid Support Forces (RSF). The city's inhabitants suffered greatly from the conflict, and women in particular sustained additional physical trauma, which is the focus of this study.

Methodology: This retrospective, cross-sectional, hospital-based study used recovered emergency room admission records from El Fasher South Hospital during the conflict period. Records were assessed for the cause, site, treatment, and short-term outcome of trauma among conflict victims, with women compared with men to determine the differential impact.

Results: Of 194 patient records reviewed, 164 were selected: 134 (81.7%) men and 30 (18.3%) women. Mean age ($\pm$ SD) of women was 30.7 ($\pm$ 11.9) years. Explosion was the commonest cause of injury in both men (54.5%) and women (63.3%), $p = 0.613$. Women sustained significantly more upper-limb injuries than men (30.0% vs. 13.4%, $p = 0.018$), whereas men had significantly more abdominal injuries than women (56.7% vs. 36.7%), $p = 0.043$. Reported early deaths occurred in four men (3.0%) and one woman (3.3%), $p = 0.641$. On multivariate analysis, independent predictors of early death included abdominal injury (adjusted OR = 0.033, 95% CI 0.008-0.136, $p < 0.001$), lower-limb injury (adjusted OR = 0.074, 95% CI 0.010-0.559, $p = 0.012$), and major surgical intervention (adjusted OR = 0.105, 95% CI 0.024-0.449, $p = 0.002$).

Discussion: Amid warfare, women face specific vulnerability to sexual violence and deteriorating maternal care. Indiscriminate bombardment of civilians also placed women at serious physical risk comparable to that faced by combatants at the frontlines.

Keywords: El Fasher city siege; wartime surgical care; women's health; conflict trauma; Sudan

Introduction

Background: The current Sudanese war broke out on 15 April 2023 in the capital, Khartoum, between the Sudanese Armed Forces (SAF) and the rebel Rapid Support Forces (RSF), and rapidly spread across most of central and western Sudan [1].

The conflict in El Fasher, capital of North Darfur State, began as a tight siege around the city and the 6th Infantry Division of the Sudanese Army. It persisted for 18 months before ending with the RSF's complete capture of the city on 26 October 2025, preceded by daily armed clashes for control between the RSF and the SAF. During this period, El Fasher became the SAF's last stronghold in Darfur [2].

Problem StatementThe El Fasher siege had a serious impact on the city's population in general, and on women in particular, as monitored by United Nations humanitarian organizations and others. Women fleeing the city reported suffering starvation, displacement, rape, and bombardment. Pregnant women gave birth in the streets after the city's remaining maternity hospitals were looted and destroyed [3].

Worldwide, women and children face considerable morbidity and mortality from armed conflict. In 2017, an estimated 36 million children and 16 million women were displaced as refugees or internally displaced persons. The number of women living near

armed conflict (within 50 km) rose from 185 million women and 250 million children in 2000 to 265 million women and 368 million children in 2017. Women of reproductive age living near high-intensity conflict have a mortality rate three times higher than women in peaceful settings [4].

Impact on Health ServicesEl Fasher had four main hospitals: Saudi Maternity Hospital, Babiker Nahar Paediatric Hospital, South Hospital, and El Fasher Teaching Hospital. El Fasher Teaching Hospital went out of service early in the crisis. The remaining hospitals struggled to serve the population despite repeated shelling, looting, and bombardment directed at facilities and staff [4]. **Literature Review:**

Impact of War on Women Worldwide, Regionally, and Locally

In 2025, the UN Secretary-General reported that 676 million women were living within 50 kilometers of deadly conflict — the highest level since the 1990s. Civilian casualties among women and children quadrupled compared with the previous two-year period, and conflict-related sexual violence increased by 87% over two years [5].

The targeting of women in El Fasher resembles patterns of “gendered warfare” observed in other regional conflicts, in which sexual violence is weaponized as a tool of ethnic cleansing, compounded by starvation

through urban sieges and the destruction of maternal healthcare infrastructure [6 - 8].

Tigray War, Ethiopia (2020–2022)

A comparable situation occurred in the Tigray conflict, where women described a “strategy of terror” involving rape and sexual violence used by soldiers to humiliate and degrade the civilian population along ethnic lines. As in El Fasher, the Tigray region was subjected to a tight siege and blockade for two years, causing mass starvation, particularly among pregnant and nursing mothers; gender-related violence affected an estimated 250,000 women [9, 10].

Syrian Civil War (2011–Present)

During the Syrian conflict, women and girls suffered extensively from food insecurity and health system collapse, particularly in Eastern Ghouta and Aleppo, in a context of siege warfare, sexual slavery, and destruction of maternity care [11, 12].

Sierra Leone Civil War (1991–2002)

This conflict involved serious, largely unrecognized crimes against women, including ethnically targeted sexual violence [13, 14].

Justification

In the midst of active warfare, limited resources and heavy workloads for insufficient staff typically constrain sound documentation and limit research.

Research Question

What was the impact of the war in El Fasher on women?

Objectives

With regard to women's surgical injuries during the El Fasher siege, this study aimed to:

- Determine selected demographic characteristics of the affected women
- Estimate the cause, presentation, and site of injuries
- Estimate reported deaths and outcomes of management
- Identify risk factors for early mortality

1. Materials and Methods

Design

Descriptive, cross-sectional, retrospective study.

Setting

- a. Study duration

The city siege period (April/May 2024 - 25 October 2025)

- b. Setting

El Fasher South Hospital

El Fasher South Hospital is a specialized governmental hospital operated by the Sudanese Ministry of Health, located in the northern part of the city. It has approximately 100 beds serving medicine and surgery, supported by laboratory and imaging services. Surgical staff comprised four general surgeons, two orthopedic surgeons, one urologist, and eight residents. Counterpart facilities included the Saudi Hospital (maternity) and the Babiker Nahar Hospital (pediatric). Surgical cases were initially referred to South Hospital. Tens of thousands of the city's population were forced to flee toward Zamzam camp in large waves due to repeated attacks on the city.

c. Study population

i. Inclusion criteria

Inclusion criteria: adult patients presenting to the hospital during the siege period.

ii.

Exclusion criteria: children, non-traumatic surgical conditions, and incomplete records.

Sampling

Surgical staff estimated total war victims presenting to the hospital at 2,000-3,000; those with mild injuries were often discharged immediately after initial treatment.

a. Sample size

All available records were reviewed for this study (sample size determined by record availability).

Data collection technique and tool

Data were collected by reviewing available patient records - structured, brief admission sheets completed by hospital medical officers and surgical residents. Data were entered into a data sheet organized into five sections: gender (2 options), age (1 item), cause of injury (3 options), site of injury (7 options), clinical status (2 options), treatment type (3 options), and early outcome (2 options).

Study variables

Independent variables were patient gender (male, female), age (years), cause of trauma (bullet, explosion, stabbing), and site of trauma (head, neck, spine, chest, upper limb, abdomen, lower limb).

Dependent variables were clinical presentation (stable, unstable), treatment type (conservative; minor operation/local

anesthesia; major operation), and early outcome (survival, death).

Minimization of Bias

This study is susceptible to recall, selection, and information bias, as exposures and outcomes are often measured simultaneously or reported from memory. Bias was minimized by retrieving data from standardized hospital short-admission records applied consistently across patients to reduce inconsistency [15-17]. Blinding could not be achieved given the limited number of records (194).

Data analysis

Continuous variables were summarized as mean $\pm$ standard deviation; categorical variables were presented as ratios and percentages. Comparisons were made using *t*-Student's t-test and the *Chi*-square test for continuous and categorical data, respectively. Univariate logistic regression was used to assess risk factors for early mortality; variables significantly associated on univariate analysis were entered into a multivariate model. A *p*-value < 0.05 was considered statistically significant. Data entry and analysis used Microsoft Excel 2021 and SPSS (IBM) version 24.

Ethical Considerations

The study was approved by the Research and Ethics Committee of the General Surgery Council, Sudan Medical Specialization Board.

2. Results:**Participants' flow chart**

Of 194 patient records reviewed for presentation to the surgical emergency unit, exclusions comprised 15 children, 8 non-

traumatic cases, 2 records with deficient information, and 5 duplicate records, leaving 164 records for analysis (see **Figure 1**).

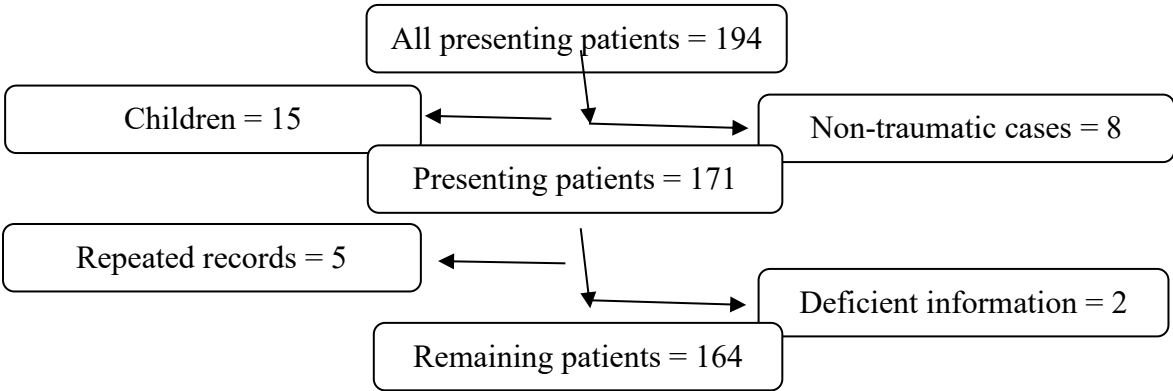


Figure 1 Selection flow of the patients presenting to the emergency unit of the El Fasher South Hospital during the siege April 24 – October 2025

Participant Characteristics

Gender and Age

Of the 164 study patients, 30 (18.3%) were women and 134 (81.7%) were men. Mean age (± SD) was 34.2 (± 14.4) years (range 15.0-86.0) in men and 30.7 (± 11.9) years (range 17.0-62.0) in women, *p* = 0.278.

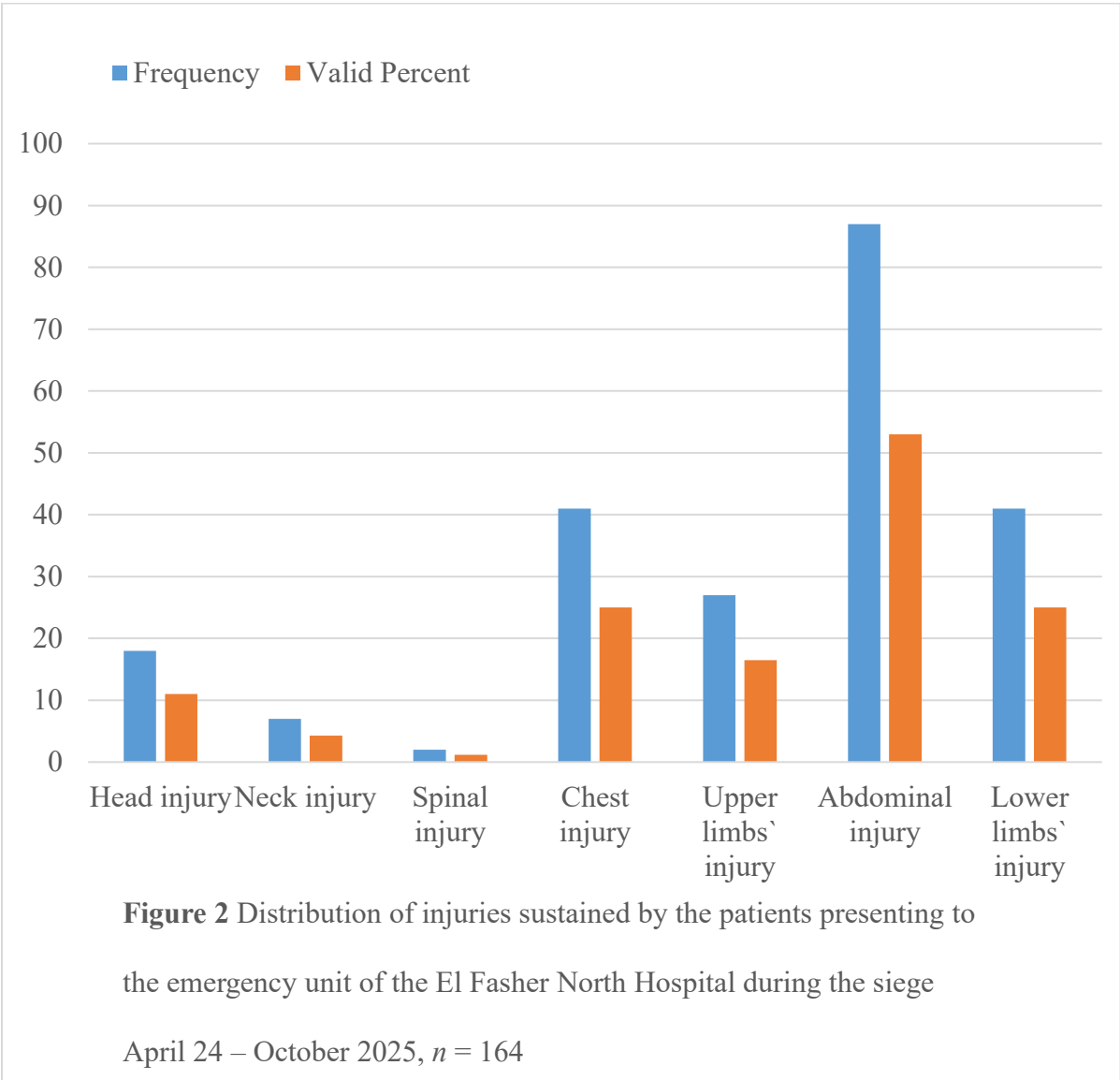
Injury Characteristics

Most patients were injured by explosions (56.1%), and 26.8% by bullets. On presentation, 43.3% were stable and 14.0% were vitally unstable (**Table 1**).

Frequency of injuries sustained by all patients to different body parts is presented in **Fig. 2**. The majority of patients (59.1%) required major operative treatment, and the overall reported early death rate was 3.0%.

Table 1 Injury Details of Patients Presenting to the Emergency Unit of El Fasher South Hospital During the Siege, April 2024-October 2025 (n = 164)			
Injury details		Frequency	Valid Percent
Injury cause	Bullet	44	26.8
	Explosion	92	56.1
	Stab injury	3	1.8
Primary survey status	Stable	71	43.3
	Unstable	23	14.0
Head injury	Yes	18	11.0

	No	145	88.4
Neck injury	Yes	7	4.3
	No	155	94.5
Spinal injury	Yes	2	1.2
	No		
Chest injury	Yes	41	25.0
	No	120	73.2
Upper limbs` injury	Yes	27	16.5
	No	135	82.3
Abdominal injury	Yes	87	53.0
	No	75	45.7
Lower limbs` injury	Yes	41	25.0
	No	122	74.4
Treatment type	Conservative or minor procedure	23	14.0
	Moderate operation	37	22.6
	Major operation	97	59.1
Treatment outcome	Survival	159	97.0
	Reported death	5	3.0



Women's Injuries Compared with Men

The commonest cause of injury was explosion in both men (54.5%) and women (63.3%) ($p=0.613$). Instability on presentation did not differ significantly between men (13.4%) and women (16.7%) ($p=0.856$). Women sustained significantly more upper-limb injuries than men (30.0% vs. 13.4%, $p=0.018$), whereas men sustained significantly more abdominal injuries than women (56.7% vs. 36.7%, $p=0.043$). No significant difference was observed between men and women in the distribution of treatment type ($p=0.083$) (see **Table 2**).

Table 2 Injuries in Women Compared with Men, El Fasher South Hospital, April 2024-October 2025 (n = 164)						
		Patient Gender				<i>P</i>
		Male <i>n</i> = 134		Female, <i>n</i> = 30		
		n	%	n	%	
Cause of injury	Bullet	37a	27.6%	7a	23.3%	0.613
	Explosion	73a	54.5%	19a	63.3%	
	Stab injury	3a	2.2%	0a	0.0%	
Status on presentation	Stable	59 _a	44.0%	12a	40.0%	0.856
	Unstable	18a	13.4%	5a	16.7%	
Site of injury	Head	14a	10.4%	4a	13.3%	0.135
	Neck	5a	3.7%	2a	6.7%	0.231
	Spinal	1a	0.7%	1a	3.3%	0.153
	Chest	33a	24.6%	8a	26.7%	0.422
	Upper limb	18a	13.4%	9b	30.0%	.018
	Abdominal	76a	56.7%	11b	36.7%	0.043
	Lower limb	31	23.1%	10	33.3%	0.059
Type of treatment	Conservative or minor procedure	19a	14.2%	4a	13.3%	0.083
	Moderate operation	27a	20.1%	10a	33.3%	
	Major operation	84a	62.7%	13a	43.3%	

Treat ment outco me	Survival	130a	97.0%	29a	96.7%	0.641
	Reporte d death	4a	3.0%	1a	3.3%	

Exact Sig. (2-sided). Significant <i>p</i> value <.05 level.
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Mortality Comparison:

The reported death rate did not differ significantly between men (3.0%) and women (3.3%) ($p= 0.641$) (see **Table 2**).

Predictors of Early Death

Univariate Analysis

Univariate logistic regression assessed independent variables as predictors of early mortality, including patient age, cause of **Table 3**.

injury, stability at presentation, site of trauma (head, neck, spine, chest, upper limb, abdomen, lower limb), and treatment type.

Multivariate Analysis

Variables significantly associated with early death on univariate analysis - upper-limb injury, abdominal injury, lower-limb injury, and treatment type - were entered into a multivariate logistic regression model (see

Table 3 Multivariate Analysis of Independent Predictors of Early Mortality, El Fasher South Hospital, April 2024 – October 2025, $n = 164$								
Variables	B	S.E	Wald	df	Sig.	Exp(B)	95% C.I. for EXP(B)	
							Lower	Upper
Upper limb injury			3.263	3	.353			
Upper limb injury (1)	-2.830	42972.476	.000	1	1.000	.059	.000	.
Upper limb injury (2)	-18.595	40192.970	.000	1	1.000	.000	.000	.
Upper limb injury (3)	-1.924	1.065	3.263	1	.071	.146	.018	1.178
Abdominal injury			22.439	1	.000			
Abdominal injury (3)	-3.404	.719	22.439	1	.000	.033	.008	.136
Lower limb injury			6.360	1	.012			
Lower limb injury (2)	-2.608	1.034	6.360	1	.012	.074	.010	.559
Treatment type			13.877	3	.003			
Treatment type (1)	-18.373	15203.908	.000	1	.999	.000	.000	.
Treatment type (2)	-2.263	1.048	4.657	1	.031	.104	.013	.812
Treatment type (3)	-2.256	.742	9.239	1	.002	.105	.024	.449
Significant p value <.05 level.								

Multivariate Analysis revealed that abdominal injury was independently associated with early mortality. Patients with abdominal injuries had significantly increased odds of early death (Adjusted OR = 0.033, 95% CI: 0.008–0.136, $p < 0.001$). Lower limb injury was also identified as a significant independent predictor of mortality (Adjusted OR = 0.074, 95% CI: 0.010–0.559, $p = 0.012$). Regarding treatment modalities, treatment type remained significantly associated with mortality in the multivariate model. Specifically, treatment type (2) was associated with reduced odds of early death (Adjusted OR = 0.104, 95% CI: 0.013–0.812, $p = 0.031$), while treatment type (3) also demonstrated a significant association with mortality reduction (Adjusted OR = 0.105, 95% CI: 0.024–0.449, $p = 0.002$). Upper limb injury did not retain statistical significance after adjustment for confounding variables in the multivariate model ($p = 0.071$).

3. Discussion:

Overall Patient Flow

In 2009, the United Nations estimated El Fasher's population at around 500,000. Before the 2023 outbreak of war, this had grown to an estimated 1.5 million, swelled by people fleeing RSF advances elsewhere. By the end of 2024, the city's population had fallen below 800,000, and by the time the RSF finally took control, it had dwindled to around 300,000. As shown in UN agencies and the Red Crescent, this sharp decline was driven by widespread displacement and mounting deaths from violence and starvation [18].

The 194 records of patients presenting for surgery during the 18-month siege, marked by near-daily battles, likely do not reflect the true number of war victims. Médecins Sans Frontières (MSF) estimated that between 10 May and 11 June alone, 1,418 wounded patients arrived at South Hospital and, subsequently, Saudi Hospital [19]. Underreporting is therefore unsurprising in such chaotic conditions, and hospitals in the city operated with fluctuating capacity throughout the siege.

Participant Characteristics

As shown in Table 1, both injured men and women presenting to the hospital were relatively young (mean age 34.2 years in men, 30.7 years in women; $p = 0.278$). This may partly reflect the evacuation of older residents from the city, which would reduce the overall burden of age-related injury complications. As expected, men outnumbered women among the injured (134 patients, 81.7%, versus 30 patients, 18.3%).

Cause of Injuries

The commonest cause of injury was explosion (92 events, 56.1%), followed by bullets (44 events, 26.8%), consistent with reports from victims surveyed by UN officials [20, 21]. Explosion injuries are often more complex due to their multi-trauma nature, which can include fractures, respiratory compromise, soft-tissue and internal organ injury, internal and external blood loss with shock, burns, and sensory impairment. This complexity arises from a combination of the primary shockwave, secondary flying fragments, tertiary blast wind, and quaternary

effects such as burns, crush injuries, and asphyxiation by dust [22]. Bullet injuries, while also multi-traumatic, tend to be more localized, typically involving soft-tissue damage and bone fracture, and require specialized management given the significant energy transfer and tissue damage involved [23].

Stability Status at Presentation

At presentation, 14% of patients were vitally unstable; this figure likely underrepresents the true severity of war injuries, since it does not capture those who died on-site or en route to hospital, particularly given that close-range blasts are frequently fatal. The unstable presentation of blast victims is clinically challenging and requires prompt, appropriate management, as instability significantly affects mortality. The Injury Severity Score (ISS) is generally the best predictor of mortality and later complications, but could not be calculated in this study because injuries in the available records were documented by anatomical region rather than the Abbreviated Injury Scale (AIS) required to derive the ISS [24].

Distribution of Injuries

Abdominal injury was the most frequent site of injury overall (53.0%), followed by chest and lower-limb injuries (25.0% each). Table 2.

Treatment

Ninety-seven patients (59.1%) underwent major operative treatment, a high proportion that reflects the severity of most injuries sustained.

Outcomes

A prior report estimated 226 deaths among 1,418 victims presenting to the Saudi and South Hospital emergency units between May and July 2024, an overall mortality rate of 15.9% [19]. This is considerably higher than the 3.0% overall mortality observed in this study (Table1). This discrepancy may reflect the fact that the city was more densely populated with civilians and displaced people during the early months of the conflict, elevating the initial death toll; later, following intense shelling, much of the population had already fled. The hospitals themselves were also subjected to heavy bombardment and gunfire on multiple occasions. Victim inflow and death rates measured over a short window of the conflict may therefore not represent overall patient flow or mortality across the full siege period, and under-documentation during periods of mass casualties should not be underestimated.

Study Limitations

An important limitation is reliance on records from a single hospital, together with the likelihood of missing records and a limited overall data volume. Some data, particularly on residence (including refugee camps) and occupation, were sometimes intentionally omitted for the safety of patients, as such information could have made them vulnerable. The regression model should be interpreted cautiously given the small number of mortality events, which may have affected model stability and produced wide confidence intervals.

4. Conclusion:

During the El Fasher siege, women suffered injury at rates comparable to men despite

generally not being present at the frontlines, reflecting the indiscriminate and severe nature of this conflict. The use of random bombardment should be strongly condemned, given the serious collateral injury it inflicts on civilians who are not combatants. Protection of the trunk and limbs should be prioritized for women and other potential bombardment victims, and evacuation of older residents may reduce shelling-related mortality. Documenting the humanitarian crisis in El Fasher and its surrounding displacement camps is a crucial step toward justice for its victims. Further studies are needed to assess the situation at other health institutions. This is among the few studies to document a historically overlooked disaster that besieged El Fasher amid a devastating nationwide war. It specifically focused on women, who faced substantial physical injury alongside other compounding risk factors during the contemporary Sudanese conflict.

5. Declarations

Declaration of Interest

We here declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of this research.

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Author Contributions

First author: topic formulation, data entry, data analysis, data interpretation, and manuscript writing.

Second, third, and fourth authors: topic formulation, instrument construction, patient management, and data collection.

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The Role of Clinical Pharmacist Educational Interventions in Optimizing the Practice of Oncology Physicians in the Treatment of Breast Cancer Patients in Yemen

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Abstract

The clinical pharmacist plays a vital role in the treatment of breast cancer patients, given several significant issues associated with breast cancer and its treatment, particularly chemotherapy. Few studies, globally or locally, have examined the impact of clinical pharmacist interventions on the management of hospitalized breast cancer patients. This study aimed to assess the impact of clinical pharmacist intervention on physicians' adherence to standard treatment guideline recommendations, by comparing adherence before and after an educational intervention. This prospective, cross-sectional, multi-center, pre-post educational interventional study was conducted at the National Cancer Control Foundation (NCCF) and the National Oncology Center (NOC), Yemen, from June 2023 to June 2024. A scientific meeting and dissemination of educational materials on updated NCCN guidelines for breast cancer treatment were conducted during the intervention phase, with pre-intervention and post-intervention assessments performed using the same 10-parameter survey covering prescribing, dispensing, and administering chemotherapy regimens and managing drug therapy-related problems (DTPs). Parameters before and after the educational intervention were compared using the paired-samples t-test, and the chi-square test was used to investigate the association between oncology physicians' adherence to updated NCCN guidelines and prescribed chemotherapy regimens. Physician adherence improved by nearly 20% in the post-intervention phase. Clinical pharmacist interventions help optimize physicians' practice in prescribing breast cancer chemotherapy regimens according to updated NCCN guideline recommendations.

Keywords: *Clinical pharmacist; educational interventions; oncology physician practice; breast cancer patients*

Introduction

Clinical pharmacists play a vital role, alongside other healthcare professionals, in the selection of appropriate medications and pharmacotherapy plans.¹⁻⁵ They provide patient care that directly influences drug-related needs, including medication effectiveness, medication safety, patient adherence, patient knowledge and education, and quality of life.^{5,6-9}

The role of the clinical pharmacist is particularly important in cancer care, helping to reduce difficulties and complications associated with cancer itself and with anticancer pharmacotherapy, such as diminished organ function, prolonged hospital stay, and polypharmacy.¹⁰ Managing these issues is essential to optimize medication safety and reduce drug-related problems, a major concern for patient safety.¹⁰⁻¹⁶ Another key role of the clinical pharmacist is deprescribing - discontinuing unnecessary or harmful medications to reduce the risk of drug-related problems, improve medication safety, optimize resource allocation, and improve the quality of care for cancer patients.^{17,18}

Medication errors made by nurses are common in general practice and can cause harm. These are avoidable events that can occur at any stage of the medication-use process, are widespread across healthcare

systems, and are linked to increased morbidity and mortality. Several strategies have been studied to reduce their occurrence, including various pharmacy-based interventions. In addition to participation in clinical rounds and meetings for direct intervention, one of the main clinical pharmacist-led interventions is educational programming, which has shown promising benefits. The two main groups targeted by such educational interventions are nurses and resident physicians. Programs include lectures, seminars, posters, practical teaching sessions, audit and feedback, and flashcards of high-risk abbreviations. Many studies incorporate educational sessions, either alone or combined with other approaches, often informed by errors identified before the intervention. Clinical pharmacist-led educational interventions may enhance the quality of life of breast cancer patients and play a crucial role in reducing medication errors, chemotherapy-related complications and adverse effects, and improving patient outcomes through targeted, evidence-based education for patients and healthcare providers. Personalized counseling, medication therapy management, management of drug-therapy problems, and staff training are effective methods for achieving therapy goals and consequently improving outcomes. Clinical pharmacist educational interventions in breast cancer -

including medication counseling, side-effect management, and adherence monitoring - significantly improve patient outcomes, quality of life, treatment adherence, and pharmacotherapy knowledge.¹⁹⁻²¹

Clinical pharmacist-led interventions, particularly patient education and counseling, play a critical role in supporting treatment adherence and improving quality of life among breast cancer patients. Structured pharmacist interventions can improve patient understanding, reduce anxiety, and support adherence to long-term therapies such as tamoxifen and other chemotherapy agents. Overall, pharmacist involvement is an integral part of oncology care, serving as both educator and long-term therapy companion.²²

Few studies, globally or locally, have evaluated the impact of clinical pharmacist interventions on the management of hospitalized cancer patients, particularly those with breast cancer, and few have evaluated clinical pharmacist participation in inpatient settings, where the complexity of cancer patients' medical conditions must be considered²³⁻³⁰. This study aimed to assess the clinical impact of clinical pharmacist educational interventions on the practice of oncology physicians regarding prescribing of breast cancer chemotherapy regimens and adherence to updated NCCN guidelines in the treatment of breast cancer patients.

Methodology

This prospective, cross-sectional, multi-center, pre-post educational

interventional study was conducted at the National Cancer Control Foundation (NCCF) and the National Oncology Center (NOC), Yemen, over 12 months, from June 2023 to June 2024.

Pre-intervention Phase

The pre-intervention study reviewed 214 medical records of breast cancer patients to assess physician adherence to updated NCCN guideline recommendations, using a pre-intervention checklist of 10 parameters: :

- (1) review of chemotherapy prescriptions by physicians;
- (2) prescribing of appropriate, effective, safe, and cost-effective chemotherapy regimens according to updated NCCN guidelines;
- (3) patient adherence;
- (4) appropriate time interval between chemotherapy cycles;
- (5) chemotherapy regimen doses calculated according to body surface area (BSA);
- (6) appropriate route and frequency of administration;
- (7) dose adjustment and drug intolerance management for specific conditions (liver or renal dysfunction);
- (8) prescription and administration of appropriate prophylactic antiemetic and other prophylactic drugs;
- (9) prescription and administration of appropriate supportive and palliative therapy; and

(10) appropriate toxicity-limiting steps to minimize chemotherapy-related problems and errors.

Educational Intervention Phase

Educational interventions targeting oncology physicians and nurses, based on the pre-intervention findings, were conducted through scientific meetings. Attendees received dissemination booklets containing the latest National Comprehensive Cancer Network (NCCN) guideline recommendations for breast cancer treatment.

Post-intervention Phase

The post-intervention study reviewed 236 medical records of breast cancer patients to assess physician adherence to updated NCCN guideline recommendations, using a post-intervention checklist containing the same 10 parameters as the pre-intervention phase.

Statistical Analysis

A Paired samples t-test was used to compare mean percentages of followed and not-followed recommendation parameters between the pre- and post-intervention phases, with statistical significance set at (P -value ≤ 0.05). The Pearson chi-square test was used to investigate the association between oncology physicians' adherence and prescribed chemotherapy regimens, at (P -value ≤ 0.05).

This study was conducted in accordance with the principles of the Declaration of Helsinki. Ethical approval was

granted by the Ethics Committee of The National Ribat University, Khartoum, Sudan, on 18 Septemberth 2019 (approval reference Ph.D/Pharm/2019/no:2). Formal approval to conduct the research on the study sample was also obtained from the institutional review board of the national oncology centers in Yemen. Informed consent was obtained from all enrolled patients; a detailed explanation of the study was provided before data collection, confidentiality was ensured, and patients were informed that the information collected was for research purposes only and that participation was entirely voluntary.

Results:

Physician Adherence to NCCN Guideline Recommendations

Pre-intervention assessment of physician adherence to NCCN guidelines was performed by reviewing 214 breast cancer patient records and showed variable adherence rates across recommendation parameters (see **(Table 1)**).

Educational interventions Following the educational intervention - comprising scientific meetings and dissemination of brochures and booklets summarizing the latest NCCN breast cancer treatment guideline updates for oncologists and nurses to improve adherence to these recommendations.

post-intervention assessment was performed on 236 patient records and showed overall improvement, with adherence rates

increasing by nearly 20% (**Table 1**). Differences in the mean percentages of not-followed recommendation parameters between the pre- and post-intervention phases are illustrated in (**Figure 1**).

Marked improvement was observed in the proportion of guideline recommendations followed of in the post-intervention phase. Review of chemotherapy prescriptions increased from 69% pre-intervention to 88% post-intervention. Prescribing of appropriate, effective, safe, and cost-effective chemotherapy per updated NCCN guidelines increased from 63% to 94%. Patient adherence improved from 58% to 92%. Appropriate timing between chemotherapy cycles improved from 62% to 85%. Correct chemotherapy dose calculation by body surface area improved from 77% to 92%. Appropriate route and frequency of administration by nurses improved from 65% to 96%. Appropriate dose adjustment for specific conditions or drug intolerance improved from 50% to 73%. Prescribing and administering appropriate prophylactic drugs remained at 100% in both phases. Prescribing and administering appropriate supportive and palliative therapy improved from 85% to 92%, and minimizing chemotherapy-related problems and errors improved from 65% to 77% (**Tables 1 and 2, Figure 1**).

Four of the 16 chemotherapy regimens (25%) prescribed by oncologists across all enrolled cases were not recommended by NCCN guidelines.

Regarding improvement in physician adherence at the post-intervention phase, there was a higher adherence rate, with successful guideline-concordant prescribing in 80% of cases.

Discussion

The clinical pharmacist intervention in this study led to improvements across parameters relating to prescribing, dispensing, and administering chemotherapy regimens, and to managing drug therapy-related problems (DTPs). These findings correspond with those of other studies on the role of clinical pharmacists in oncology settings.³¹⁻³³ Consistent with our study design and findings, a recent study³¹ found that clinical pharmacist educational interventions improved healthcare professionals' knowledge and, consequently, their practice in prescribing and administering intravenous chemotherapy for cancer patients.

A consistent regional study conducted in Iraq³⁴ showed that clinical pharmacist interventions are critical in reducing complications and adverse effects associated with breast cancer chemotherapy, and significantly increased patients' knowledge, attitudes, and practices regarding chemotherapy.

Clinical pharmacists significantly improve oncologists' and other healthcare practitioners' adherence to updated chemotherapy guidelines, with similar studies showing increased compliance with treatment protocols and documentation.

Through multidisciplinary collaboration, they reduce chemotherapy errors, manage adverse effects, and optimize dosing, thereby enhancing overall patient safety. Pharmacist-led interventions also improve adherence to oral anticancer medication regimens, and clinical pharmacists play a key role in implementing and reviewing updated, evidence-based chemotherapy protocols, particularly for oral oncolytics.³⁵

An Egyptian study¹⁹ reported similar findings, with pharmacist interventions producing a significant reduction in nurse medication error rates, from 34.2% pre-intervention to 15.3% post-intervention ($p < 0.001$), with declines observed across all error types. Clinical pharmacist interventions effectively improved nurses' drug knowledge and error awareness, reducing both the rate and severity of medication administration errors in an emergency hospital setting. Educational programs led by clinical pharmacists were associated with significant reductions in the overall rate of prescription and administration errors.²⁰

Clinical pharmacist interventions improved functional domains (physical, role, emotional, cognitive, and social) for breast cancer patients in an Iraqi study, with significant improvement following intervention, while fatigue, nausea/vomiting, and pain symptoms significantly decreased.²¹ Improvements were seen across several quality-of-life domains, including physical, emotional, and social functioning; however,

some studies report inconsistent findings, particularly regarding statistical significance, potentially reflecting differences in sample size, intervention duration, and other factors such as family support and disease prognosis.²²

Health-related quality of life and reduction of side effects play an important role in cancer treatment. Clinical pharmacist interventions have been shown to improve clinical outcomes for breast cancer patients, with significant reductions in toxicity grades - for example, grade 2 anemia decreasing from 17% to 1.7%, and grade 4 nausea/vomiting decreasing from 5% to 0% - along with improvement in mean quality-of-life scale scores, such as systemic therapy side-effects scores decreasing from 80.8 ± 19.53 to 42.8 ± 16.8 (all $p < 0.001$).³⁶

A clinical oncology pharmacy survey reported a high response rate, with all participants reporting involvement in one or more clinical oncology pharmacy tasks; the highest response rates were for patient counseling (62.5% actively counseling outpatients) and drug-drug interaction checking (58%). Nearly 50% of participants reported that their interventions were always or usually accepted by physicians.³⁷

Pharmacist-led interventions have shown a positive impact on breast cancer management and health outcomes. Clinical pharmacists commonly provide chemotherapy consultation, risk assessment and patient education, detection of adverse

drug reactions and drug-drug interactions, and adherence assessment, with benefits including better quality of life, reduced drug interaction risk, greater adherence, and improved patient knowledge - confirming the importance of including clinical pharmacists on the oncology team caring for breast cancer patients.³⁸

A recent, consistent study³⁹ evaluated the clinical and financial impact of clinical pharmacist interventions and pharmacist-driven cost savings in an inpatient oncology setting, reporting significant clinical and financial impact, with a high rate of intervention acceptance by oncology physicians resulting in therapy changes such as dose adjustment and drug addition or discontinuation.

Regarding breast cancer awareness, a regional pre-post study⁴⁰ reported improved awareness of breast cancer symptoms, risk factors, and diagnostic techniques among participants ($p = 0.000$). Breast self-examination practice increased significantly during the post-intervention phase (from 2.5% to 93.8%), knowledge of clinical breast examination improved from 8.5% to 84.4%, and understanding of mammography as a screening technique improved significantly, with approximately 34.7% of eligible women having undergone mammography post-intervention.

Mean adherence to various clinical pharmacist recommendations in cancer treatment guidelines has been reported to

range from 40% to 99% across studies, differing substantially by cancer type and treatment modality, with higher adherence for breast cancer and melanoma recommendations and relatively lower adherence for lung cancer or chemotherapy/radiotherapy-related recommendations.⁴¹

Regarding physician adherence to chemotherapy guidelines, greater adherence to American Society of Clinical Oncology guidelines has been associated with high emetogenic-risk regimens ($p = 0.012$), hematological malignancies ($p = 0.005$), and use of two or more chemotherapy regimens ($p = 0.05$), while paclitaxel-based treatment was the only significant risk factor for non-adherence ($p = 0.02$).⁴²

Oncology pharmacists are vital members of the multidisciplinary team in Hong Kong hospitals, contributing to medication selection, prescribing, procurement, monitoring, and education for cancer patients. Their professional drug knowledge adds value to the multidisciplinary team and promotes the rational use of anticancer treatment, which is highly valued by other healthcare professionals.⁴³

Clinical pharmacy services may optimize therapy effectiveness and prevent adverse effects and non-adherence. Pharmacist interventions were highly acknowledged by oncologists and patients in a study from Northern Cyprus, suggesting

substantial value in implementing clinical pharmacy services in additional hospitals in the region.⁴⁴

Clinical pharmacy interventions in oncology are critical for optimizing chemotherapy specifically, reducing medication errors, and managing side effects such as pain, gastrointestinal distress, and cardiovascular adverse reactions. Clinical pharmacists facilitate the adoption of the latest treatment guidelines and can detect and prevent significant prescribing errors, reported to range from 4.7% to 6.1% in chemotherapy and investigational drug settings; typical interventions include dose adjustment, addition of supportive care, and management of drug-drug interactions, improving patient safety and yielding substantial financial savings through reduced length of stay and cost avoidance.^{36, 45-47}

Multi-center international studies⁴⁸⁻⁴⁹ have confirmed the positive clinical significance of pharmacist interventions in oncology and the importance of pharmacist collaboration with other healthcare practitioners for optimizing chemotherapy protocol selection, individualizing chemotherapy doses, improving treatment safety, preventing medication errors, and increasing adherence to evidence-based chemotherapy guidelines.

Conclusion

Clinical pharmacist interventions improved clinical outcomes for breast cancer

patients, in collaboration with oncology physicians and nurses, by improving prescribing, dispensing, and administering of chemotherapy regimens, addressing chemotherapy-related needs, managing drug therapy-related problems, and improving both patients' medication-use adherence and physicians' adherence to updated NCCN breast cancer chemotherapy protocols. Clinical pharmacists should be incorporated into the multidisciplinary healthcare team at local Yemeni oncology centers to provide oncology services to both healthcare professionals and cancer patients, particularly those with breast cancer.

Declaration of Interest

There is no reported conflict of interest that could be perceived as prejudicing the impartiality of the research.

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Author Contributions

The first draft of the manuscript was written by all authors, and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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Tables:

Table (1): Percentages of not followed recommendations parameters in pre-intervention phase (N=214) and post-intervention phase (N=236)

No.	Recommendation parameters	Not followed Pre-intervention	Not followed Post-intervention
		%	%
1	Reviewing of chemotherapy regimens prescriptions by physicians	31%	12%
2	The appropriate, effective, safe and cost-effective chemotherapy regimens prescribed according to updated NCCN guidelines	37%	6%
3	Patient adherence	42%	8%
4	The appropriate time between chemotherapy cycles	38%	15%
5	Chemotherapy regimen doses according to body surface area (BSA)	23%	8%
6	The appropriate route and frequency of administration	35%	4%

7	Dose adjustment and drug intolerance for specific conditions (liver or renal dysfunction)	50%	27%
8	The prescription and administration of appropriate prophylactic antiemetic drugs and other prophylactic drugs	0	0%
9	The prescription and administration of appropriate supportive and palliative therapy	15%	8%
10	Taking appropriate specific toxicity-limiting steps to minimize chemotherapy problems and errors	35%	23%

Table (2): The mean difference of percentages of followed and not followed recommendations parameters between pre-intervention phase and post-intervention phase using paired samples t-test

Parameters	Pre-intervention phase	Post-intervention phase	P-value Sig. (2-tailed)
Followed (Physician adherence)	69	89	0.001*
Not Followed)Physician non-adherence(	31	11	0.001*

*Significant difference (P-value $\leq$ 0.001) between means of the two phases

Figures:

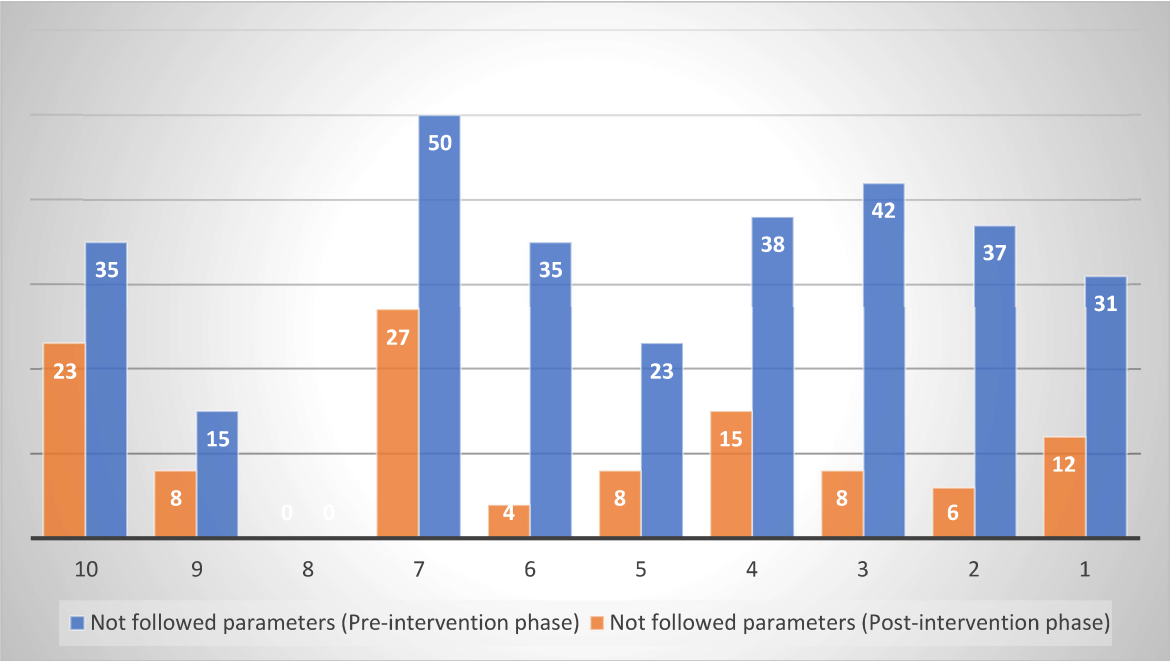


Figure (1): Differences in percentages of not followed recommendations parameters between pre-intervention phase and post-intervention phase

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