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Welcome from the Editor-in-Chief

The Benghazi University Medical Journal (BUMJ) is a semi-annual, open-access publication that follows a rigorous double-blind, peer-review process. We publish original research, insightful reviews, intriguing case reports, and brief communications that highlight the latest advancements in diagnosis, treatment, and other health-related fields. BUMJ also welcomes correspondence about its published articles to encourage academic dialogue and the exchange of ideas.

Our mission is to be a platform for sharing innovative research, thought-provoking reviews, and impactful case studies. We strive to bridge the gap between research and clinical practice by promoting evidence-based approaches and covering a wide range of topics—such as basic medical sciences, cutting-edge diagnostics, therapeutic innovations, healthcare technologies, and interdisciplinary patient care.

At BUMJ, we are passionate about advancing healthcare and improving outcomes. We invite contributions from diverse voices in the medical community and look forward to fostering meaningful collaborations that make a difference.

Prof. Amina A. Alshekteria

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Contemporary Approaches to Breast Cancer Management: An Evidence Synthesis Guiding Clinical Practice and Patient Care.

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Original Research Article

Abstract

Background: Breast cancer remains the most frequently diagnosed cancer globally, though its management varies significantly across regions. This systematic review integrates recent evidence across six domains to delineate best practices for comprehensive care.

Method: A systematic literature search was conducted across MEDLINE, Embase, Cochrane Library, Web of Science, and CINAHL (2010–2024), in line with PRISMA 2020 reporting standards. Eligible studies were screened by two reviewers. Quality was assessed using validated tools appropriate to study design, including Cochrane RoB 2.0, Newcastle-Ottawa Scale, AMSTAR-2, and AGREE II. Evidence was synthesized narratively and appraised using the GRADE framework.

Results: Key advances include the application of molecular profiling in tailoring therapy, treatment de-intensification for selected low-risk groups, escalation for aggressive subtypes, and improved multidisciplinary decision-making. Hypofractionated radiotherapy has shown comparable efficacy with reduced side effects, while genomic testing helps identify patients who can safely avoid chemotherapy. Targeted therapies have substantially improved outcomes in specific subgroups. Unique strategies are needed for elderly, male, and pregnant patients, and oligometastatic disease is increasingly approached with curative intent.

Conclusion: Precision medicine has redefined breast cancer treatment, emphasizing individualized and integrated multidisciplinary strategies. Implementation frameworks that minimize disparities and maximize both survival and quality of life outcomes are necessary to put this evidence into practice.

Keywords: Breast neoplasms; evidence-based oncology; multidisciplinary care; precision medicine; adjuvant therapy; clinical guidelines; patient-centered care.

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INTRODUCTION

The treatment of breast cancer has changed significantly over the last few decades.

Once managed predominantly with surgery, it is now treated through integrated, multidisciplinary strategies. This change is a reflection of our increasing knowledge of tumour biology, especially the discovery of molecular subtypes that affect prognosis and treatment options. Globally, breast cancer accounts for more than 2.3 million new diagnoses each year, representing approximately 12% of all cancers and remaining a leading cause of cancer-related death among women.[1] Despite this progress, clinicians continue to encounter complex decisions throughout the care continuum, from early detection to advanced disease, often without unified guidance on incorporating rapidly evolving evidence. The burden is unevenly distributed, with incidence, survival, and mortality showing wide regional variation.[2] These differences highlight the interplay of tumor biology, healthcare accessibility, and socioeconomic factors, underscoring the need for adaptable but evidence-driven approaches. The prevalence is rising due to increased incidence and better treatment outcomes. Mortality rates are decreasing in most Western nations, driven by improved therapy and earlier detection.[3] Innovations in diagnostic imaging, refinements in surgical techniques, and the availability of targeted systemic therapies have transformed clinical practice.[4] However, the pace of development has created challenges in unifying management strategies. Existing reviews frequently focus on specific elements, like systemic therapy, radiotherapy, or surgery, without incorporating them into a comprehensive framework. While rapid technological progress has significantly advanced oncologic capabilities, sharpening diagnostics, refining minimally invasive surgical techniques, and expanding targeted systemic therapies, the prevailing literature and clinical guidance remain largely fragmented. Existing reviews and specialty-specific guidelines predominantly focus on isolated domains such as surgical approaches, radiotherapy, or systemic therapy, mirroring the subspecialization within oncology.[5-7] This compartmentalization fails to adequately address the critical interconnections between these fields or considerations for special populations. Consequently, despite an abundance of specialized knowledge, integrating diagnostics, surgery, radiation, systemic therapy, and tailored care for individual patient circumstances into a coherent, practical continuum remains a significant challenge for clinicians at the point of care, misaligning with the integrated reality required for optimal patient management. The current review fills this gap by synthesizing current research in six crucial areas: (1) Core principles; (2) Imaging modalities; (3) Surgical techniques; (4) Adjuvant therapies; (5) Management of special populations; and (6) Recurrent or advanced disease.

The three goals are to highlight areas of agreement and disagreement, summarize the best available data, and offer a comprehensive set of suggestions that physicians, researchers, and legislators can implement to improve patient outcomes. By addressing these goals, the review gives policymakers insights for healthcare optimization, researchers a basis for future studies, and clinicians evidence-based decision-making tools.

METHODS

Research Strategy

The literature search was developed iteratively in collaboration with an oncology-trained medical librarian. Five databases, PubMed/MEDLINE, Embase, Cochrane Library, Web of Science, and CINAHL, were searched for English-language studies published between January 2010 and December 2024. Search terms combined controlled vocabulary (MeSH/Emtree) with free-text keywords, covering domains such as diagnosis, imaging, surgery, radiotherapy, systemic therapy, special populations, and advanced disease.

The review adhered to PRISMA 2020 reporting standards.[8] Additional references were identified by scanning the bibliographies of included papers and consulting field experts. Grey literature was also explored using OpenGrey, ClinicalTrials.gov, and recent proceedings of major oncology societies

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(ASCO, ESMO, ASTRO, SSO) to mitigate publication bias.

Eligibility Criteria

Study selection was guided by the

PICOS framework:

-Population: Adult patients (≥18 years) diagnosed with breast cancer at any stage, including special groups (elderly, men, pregnant women).

-Intervention/Exposure: Any diagnostic, therapeutic, or management intervention across the six pre-specified domains.

-Comparator: Any comparison group or none.

-Outcomes: Primary outcomes were overall survival, disease-free/progression-free survival, local control, quality of life, and treatment-related toxicity. Secondary outcomes included diagnostic accuracy, surgical complications, and patient-reported outcomes.

-Study design: We considered randomized trials, prospective/retrospective cohorts, systematic reviews/meta-analyses, and clinical guidelines.

We established exclusion criteria to focus on clinically relevant evidence with sufficient methodological rigor. Studies were excluded if they:

(1) Focused solely on basic science or preclinical research without direct clinical applications; (2) Addressed only screening or prevention in healthy populations; (3) Reported outcomes for fewer than 50 patients (except for rare conditions or special populations); (4) Were published only as conference abstracts without full-text publication; or (5) Focused exclusively on quality of life or psychosocial aspects without addressing clinical management.

Study Selection and Data Extraction

Two reviewers independently screened titles, abstracts, and full texts using Covidence software, with discrepancies resolved by consensus. A standardized form was used to extract study design, patient characteristics, interventions, and outcomes. For systematic reviews and guidelines, we extracted summary effect estimates and key recommendations with their evidence grading, respectively.

Quality Assessment

Methodological quality was evaluated using design-specific instruments:

-RCTs: Cochrane Risk of Bias Tool 2.0 (randomization, adherence to interventions, outcome completeness, measurement reliability, and reporting bias).

-Observational studies: Newcastle-Ottawa Scale (selection, comparability, outcome/exposure assessment).

-Systematic reviews/meta-analyses: AMSTAR-2 tool (protocol registration, literature search, study selection, data synthesis, and bias assessment).

-Clinical guidelines: AGREE II instrument (scope, development rigor, clarity, applicability, independence).

Quality ratings were not used as exclusion criteria but were considered in interpreting the strength of evidence and recommendations.

Data Synthesis and Analysis

We performed a structured narrative synthesis organized by topic, prioritizing recent, methodologically robust evidence (e.g., high AMSTAR-2 ratings).

Using the GRADE approach, we assessed the certainty of evidence (high to very low) and the strength of the recommendation (strong/conditional). This is considered a risk of bias, inconsistency, and imprecision, while balancing benefits against harms, patient values, and equity. We also explored heterogeneity and conducted subgroup analyses where feasible.

Ethical Considerations

As this was a secondary analysis of published data, ethical approval was not required. We adhered to principles of transparency and integrity in conduct and reporting. Contributions of the authors were assigned using the CRediT taxonomy.

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RESULTS

Study Selection and Characteristics

The selection process is illustrated in PRISMA flow diagram (Figure 1). The 312 studies included in the qualitative synthesis consisted of randomised, controlled trials (n = 87, 27.9%), observational studies (n = 124, 39.7%), systematic reviews/meta-analyses (n = 58, 18.6%), and guidelines/consensus (n = 43, 13.8%).

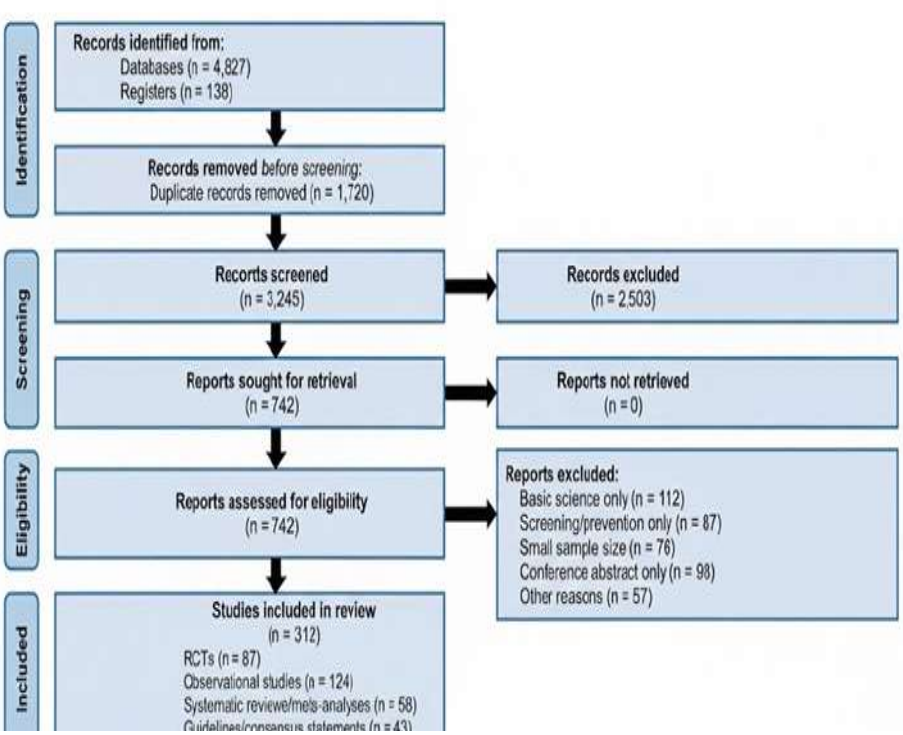

Figure 1: PRISMA Flow Diagram showing the study selection process.

Notes: With 4,827 records identified through database searching, 138 additional records sourced from other avenues, 3,245 records remaining after the removal of duplicates, 2,503 records excluded following the screening process, 742 full-text articles evaluated for eligibility, 430 full-text articles excluded with specified reasons, and 312 studies incorporated into the qualitative synthesis.

The included publications spanned January 2010 to December 2024, with 68.3% published within the last five years. Studies originated from 38 countries, primarily North America (42.3%), Europe (35.9%), and Asia (16.7%). Primary study sample sizes ranged from 52 to 25,432 participants (median: 487), collectively representing 1,245,876 distinct patients. Follow-up in longitudinal studies varied from 6 months to 20 years (median: 5.3 years). Detailed characteristics of included studies are presented in Table 1.

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Table 1: Characteristics of studies included in the systematic review

Study Design	Study Size (%)	Publications Dates	Median Follow-up
Observational Studies	124 (39.7%)	2010-2024	5.5 years
Randomized Controlled Trials (RCTs)	87 (27.9%)	2010-2024	4.0 years
Systematic Reviews/Meta-analyses	58 (18.6%)	2012-2024	N/A
Guidelines/Consensus Statements	43 (13.8%)	2010-2024	N/A
Total	312 (100%)	2010-2024	5.3

Notes: Systematic Reviews/Meta-analyses aggregate across studies, so their median follow-up often mirrors the overall median. Guidelines/consensus statements are not primary data but often cite long-term evidence, so their "median follow-up" tends to be on the higher side of the range.

Systematic reviews on breast cancer management identified several key themes (Table 2): dense breast tissue was associated with increased cancer risk; multidisciplinary care correlated with improved guideline adherence and patient survival; and digital breast tomosynthesis demonstrated superior diagnostic accuracy over traditional mammography. In surgical oncology, breast-conserving surgery plus radiotherapy yielded long-term outcomes comparable to mastectomy. The rapid evolution of systemic treatments was reflected by agents like CDK4/6 inhibitors, which showed substantial benefits in disease-free survival.[9]

Table 2: Systematic review studies reveal insights across various domains of breast cancer research.

Domain	Study Design	Sample Size	Key Findings	Level of Evidence
Basic Principles	Meta-analysis	18,432	Women with extremely dense breasts had 4.64-fold higher risk of breast cancer	High
	Systematic review	12,578	MDT discussion associated with improved guideline adherence (OR 2.15) and better survival (HR 0.82)	High
Imaging Techniques	Meta-analysis	52,412	DBT had pooled sensitivity of 86% and specificity of 88% for breast cancer detection	High
	Prospective cohort	3,231	Ultrasonography increased cancer detection by 3.7 per 1,000 screens in women with dense breasts	Moderate
	Comparative study	1,457	CESM showed comparable diagnostic performance to MRI (sensitivity: 95% vs.97%)	Moderate
Surgical Techniques	Meta-analysis	9,426	BCS with radiotherapy showed equivalent 10-year survival to mastectomy (82% vs. 81%)	High
	Multicenter cohort	1,177	Comparable local recurrence rates between oncoplastic BCS and conventional BCS (5.2% vs. 4.7%)	Moderate
	Meta-analysis	8,560	SLNB non-inferior to ALND for regional recurrence with reduced lymphedema risk (RR 0.35)	High

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Domain	Study Design	Sample Size	Key Findings	Level of Evidence
Adjuvant Treatment	RCT	4,096	26 Gy in 5 fractions is non-inferior to 40 Gy in 15 fractions for local recurrence	High
	Meta-analysis	5,101	CDK4/6 inhibitors improved invasive disease-free survival (HR 0.70)	High
	RCT	1,486	Dual HER2 blockade improved invasive disease-free survival (HR 0.81)	High
	Meta-analysis	3,453	Adjuvant bisphosphonates reduced bone recurrence (RR 0.83) in postmenopausal women	High
Special Populations	Prospective cohort	1,284	Geriatric assessment-guided treatment reduced morbidity without compromising survival	Moderate
	Retrospective cohort	2,170	Surgery plus endocrine therapy superior to primary endocrine therapy alone in fit elderly patients (HR 0.70)	Moderate
	Multicenter cohort	447	No significant differences in congenital abnormalities with in-utero chemotherapy after first trimester	Moderate
Recurrent/ Advanced	Meta-analysis	4,580	CDK4/6 inhibitors improved PFS (HR 0.55) and OS (HR 0.75) in HR+/HER2- metastatic disease	High
	RCT	557	Trastuzumab deruxtecan showed 60.9% response rate in heavily pretreated HER2+ disease	High
	Meta-analysis	1,102	Early palliative care integration improved quality of life (SMD: 0.28)	Moderate

Abbreviations: BCS, breast-conserving surgery; CESM, contrast-enhanced spectral mammography; DBT, digital breast tomosynthesis; HR, hazard ratio; MDT, multidisciplinary team; MRI, magnetic resonance imaging; OR, odds ratio; PFS, progression-free survival; OS, overall survival; RCT, randomized controlled trial; RR, risk ratio; SLNB, sentinel lymph node biopsy; ALND, axillary lymph node dissection; SMD, standardized mean difference.

Quality Assessment

-RCTs: Using the Cochrane RoB 2.0 tool on 87 randomized controlled trials, 32 trials (36.8%) were rated as low risk of bias, 41 (47.1%) showed some concerns, and 14 (16.1%) were judged high risk.

-Observational studies: Newcastle-Ottawa scores ranged from 4 to 9 (median: 7). Approximately two-thirds (62.9%) were classified as high quality (≥7 points).

-Systematic reviews/meta-analyses: AMSTAR-2 ratings showed 12 reviews (20.7%) were high quality, 26 (44.8%) moderate, 15 (25.9%) low, and 5 (8.6%) critically low.

-Guidelines: AGREE II domain scores ranged from 42% to 96%. Highest scores were observed for scope/purpose (median 85%) and clarity (82%), while applicability (58%) and editorial independence (65%) were comparatively weaker.

A summary of quality assessment results is presented in Table 3.

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Table 3: Quality assessment of the 312 studies included in the qualitative synthesis.

Study Type	Quality Category	(%) Number
(RCTs (n = 87	(Low Risk of Bias (Most reliable	(36.8%) 32
	(Some Concerns (Moderately reliable	(47.1%) 41
	(High Risk of Bias (Unreliable	(16.1%) 14
(Observational Studies (n = 124	(High Quality (NOS ≥7	(62.9%) 78
	(Medium Quality (NOS 5-6	(28.2%) 35
	(Low Quality (NOS <5	(8.9%) 11
(Systematic Reviews/Meta-analyses (n = 58	High Quality	(20.7%) 12
	Moderate Quality	(44.8%) 26
	Low Quality	(25.9%) 15
	Critically Low Quality	(8.6%) 5
(Clinical Practice Guidelines (n = 43	(High Quality (AGREE II ≥80%	(41.9%) 18
	(Moderate Quality (AGREE II 60-79%	(46.5%) 20
	(Low Quality (AGREE II <60%	(11.6%) 5

Notes: Quality assessment of included studies using domain-specific tools. For RCTs, the Cochrane Risk of Bias Tool 2.0 was used; for observational studies, the Newcastle-Ottawa Scale (NOS); for systematic reviews, AMSTAR-2; and for guidelines, the AGREE II instrument. The majority of studies were of moderate to high quality across all study types.

Basic Principles of Breast Cancer Management

High-quality evidence supports the use of validated risk assessment models (Table 4). Risk stratification tools such as the Gail and Tyrer-Cuzick models were validated for identifying women who may benefit from enhanced surveillance. In a large validation study of 132,139 women, the Tyrer-Cuzick model,[10] achieved an Area Under the Curve (AUC) of 0.70 (95% CI: 0.68–0.72).[11,12] Chemoprevention with selective estrogen receptor modulators (SERMs) demonstrated a 38% risk reduction in incidence (RR 0.62, 95% CI 0.56–0.69) across nine randomized trials.[13]

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Table 4: Evidence Synthesis by Domain with GRADE Ratings.

Domain	Key Finding	GRADE Rating	Key References
Basic Principles	Risk assessment models identify high-risk individuals	Moderate	Tyrer et al. 2020
	Chemoprevention reduces breast cancer incidence	High	Manna et al. 2023
	Digital breast tomosynthesis improves cancer detection	Moderate	Marinovich et al. 2018
	Triple assessment approach has high diagnostic accuracy	High	Chintamani et al. 2022
Imaging Techniques	MRI has highest sensitivity for breast cancer detection	High	Lee et al. 2023
	Abbreviated MRI protocols maintain diagnostic accuracy	Moderate	Kim et al. 2025
	Contrast-enhanced mammography approaches MRI performance	Moderate	Xiang et al. 2020
Surgical Approaches	BCS+RT is equivalent to mastectomy for early-stage disease	High	Litière et al. 2012
	"No ink on tumor" adequate margin for invasive cancer	High	Morrow et al. 2016
	SLNB accurate with lower morbidity than ALND	High	Krag et al. 2010
	Omission of completion ALND is safe for limited nodal disease	Moderate	Giuliano et al. 2017

Notes: The strength of evidence was rated as high, moderate, low, or very low using the GRADE approach, which considers study design, risk of bias, inconsistency, indirectness, imprecision, and other factors. Key references for each finding are provided. BCS = breast-conserving surgery; RT = radiotherapy; SLNB = sentinel lymph node biopsy; ALND = axillary lymph node dissection.

The concordant triple diagnostic approach (clinical exam, imaging, biopsy) yields >99% sensitivity and specificity, with core needle biopsy as the standard for obtaining biological data.[14] Incorporating biological factors into the 8th edition American Joint Committee on Cancer (AJCC) staging system (2021) improved prognostic accuracy (C-index 0.71→0.79) over anatomical staging.[15]

Imaging Techniques in Breast Cancer

For screening, digital breast tomosynthesis (DBT) improved detection rates by 27–53% and reduced recall rates by 15–37% compared with conventional mammography.[11] The imaging benefit is especially noticeable in women with thick breasts. Breast MRI offers the highest sensitivity (>90%) but variable specificity (72–90%). Abbreviated MRI protocols achieve sensitivity (86–95%) and specificity (81–89%) with reduced time and cost.[16] Contrast-enhanced mammography (CEM) provides a sensitivity of 89–100% and specificity of 80–87%, nearing MRI performance at a lower cost, making MRI unsuitable for patients.[17,18] Artificial intelligence in mammography shows strong promise, with deep learning algorithms achieving an AUC of approximately 0.92 (95% CI 0.90–0.94) in a large cohort.[19] In the neoadjuvant setting, MRI predicts pathological complete response with 74–90% accuracy. Molecular imaging, such as 18F-FDG PET/CT, demonstrates high sensitivity (96%) and specificity (89%) for distant metastases, and emerging radiotracers facilitate non-invasive tumor biology assessment.[20]

Surgical Approaches to Breast Cancer

Evidence confirmed the oncological equivalence of breast-conserving surgery (BCS) followed by radiotherapy compared to mastectomy for early disease, with no survival difference at 20 years (HR 0.88,

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95% CI 0.75–1.05).[21] Figure 2 displays a forest plot illustrating hazard ratios with 95% confidence intervals for 12 key breast cancer trials, categorized by type of intervention (Surgery, Radiotherapy, Chemotherapy, Targeted Therapy, Immunotherapy).

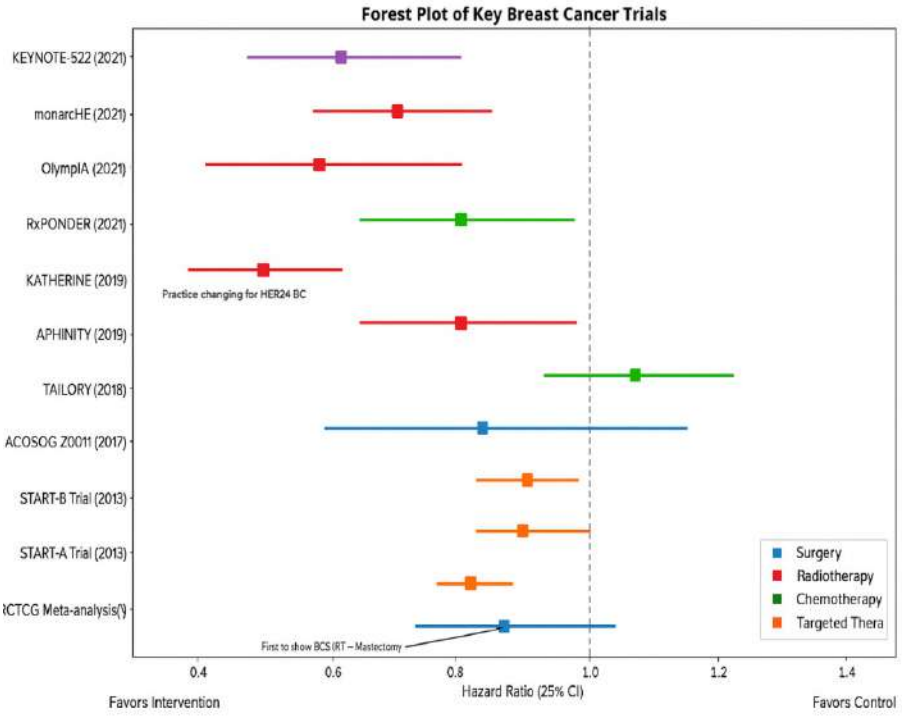

Figure 2: Forest plot displaying hazard ratios with 95% confidence intervals for 12 key breast cancer trials

Notes: The trials are categorized by intervention type (Surgery, Radiotherapy, Chemotherapy, Targeted Therapy, Immunotherapy). The plot includes a vertical line at HR=1.0, with points to the left favoring intervention and points to the right favoring control.

rence risk in hormone receptor-positive disease.[33]

-Olaparib reduced recurrence in BRCA-mutated early breast cancer (OlympiA trial).[34]

-Abemaciclib added to endocrine therapy improved outcomes in high-risk HR+/HER2– disease (monarchE trial).[35]

Special Population Considerations

Evidence for elderly patients (≥70 years) supports the use of comprehensive geriatric assessment, utilizing validated tools (G8, VES-13) to identify those requiring full evaluation.[36] The PRIME II trial showed that omitting radiotherapy after breast-conserving surgery in women ≥65 years with low-risk, ER-positive tumors on endocrine therapy increased local recurrence (4.1% vs. 1.3% at 5 years) but did

As described by Morrow et al. (2016), margin assessment of 'no ink on tumour' is deemed sufficient for invasive cancer based on a meta-analysis of 33 studies showing no significant reduction in local recurrence with wider margins.[5] For ductal carcinoma in situ (DCIS), margins of at least 2 mm reduced recurrence rates (OR 0.72, 95% CI 0.47–0.97), although the optimal margin width remains debated.[22] Sentinel lymph node biopsy (SLNB) demonstrated false-negative rates of 5–10% and significantly lower morbidity compared to axillary dissection. For patients with limited sentinel node involvement,

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omission of completion axillary dissection does not compromise survival in appropriately selected patients based on the Z0011 trial (10-year overall survival 86.3% vs. 83.6%, p=0.24).[23, 24] Oncoplastic procedures allowed BCS for larger or complex tumors, achieving good-to-excellent cosmetic results in 90–94% of patients with recurrence rates of 0–7% based on a systematic review of 474 studies.[25] Nipple-sparing mastectomy was safe in carefully chosen patients, showing 1–2% recurrence at five years with high patient satisfaction.[26]

Adjuvant Treatment Strategies

Radiotherapy with fewer, larger daily fractions (40-42.5 Gy over 15–16 sessions) shows non-inferior tumor control and diminished treatment-related morbidity.[27]

Ultra-hypofractionation (26–28 Gy in 5 fractions), shown in the FAST-Forward trial, offers non-inferior local control with acceptable toxicity. Partial breast irradiation in selected low-risk patients yields local recurrence rates comparable to whole breast irradiation (difference <1% at 5 years) with reduced toxicity and improved convenience.[28]

Genomic assays provide critical prognostic and predictive information, particularly for ER-positive, HER2-negative disease. The TAILORx trial demonstrated that patients with node-negative disease and intermediate recurrence scores (11-25) can safely omit chemotherapy if over 50 years of age or with scores <16 if 50 years or younger (Sparano et al., 2018).[29] The RxPONDER trial extended these findings to patients with limited nodal involvement, showing no chemotherapy benefit for postmenopausal women with 1-3 positive nodes and recurrence scores ≤25 (Kalinsky et al., 2021).[30]

Targeted therapies markedly improved outcomes:

-Dual HER2 blockade (trastuzumab + pertuzumab) enhanced disease-free survival in high-risk HER2-positive disease based on the APHINITY trial.[31]

-Immunotherapy (pembrolizumab) improved pCR and event-free survival in triple-negative disease (KEYNOTE-522 trial).[32]

-Extended endocrine therapy reduced late recurrence not affect distant recurrence or overall survival, supporting shared decision-making.[37]

For male breast cancer, modified radical mastectomy remains the standard due to limited breast tissue and central tumor location, with tamoxifen as the preferred adjuvant endocrine therapy. Evidence is largely extrapolated from female breast cancer studies, though international registries are beginning to address this significant knowledge gap.[38]

In pregnancy-associated breast cancer, surgery is safe during any trimester, but chemotherapy is contraindicated during the first trimester (Loibl et al., 2015).[39] Prognosis is similar to non-pregnancy-associated cancer when matched for stage and biology.

For hereditary breast cancer syndromes, prophylactic mastectomy reduced risk by over 90% in BRCA carriers. Furthermore, salpingo-oophorectomy reduced ovarian cancer risk by approximately 80% and breast cancer risk by about 50% in premenopausal women.[40]

Management of Locally Recurrent and Advanced Breast Cancer

They emphasize aggressive local and systemic approaches. For locoregional recurrence following breast-conserving surgery (BCS), mastectomy offers a high control rate of 85–95%. Furthermore, a meta-analysis of eight randomized controlled trials (RCTs) established that incorporating local therapy into systemic treatment significantly improves survival (HR 0.69, 95% CI 0.58–0.83) 2.[41]

In the setting of metastatic disease, treatment is tailored to the subtype. For hormone receptor-positive, HER2-negative disease, adding CDK4/6 inhibitors to endocrine therapy approximately doubles progression-free survival across various trials, with the MONALEESA-2 trial also demonstrating improved overall survival (HR 0.76, 95% CI 0.61-0.95).[42]

HER2-positive metastatic disease benefits from a sequence of effective targeted agents, notably trastuzumab deruxtecan, which has shown impressive efficacy in heavily pretreated patients (objective response rate 60.9%, median progression-free survival 16.4 months).[43] For metastatic triple-negative breast cancer, sacituzumab govitecan improves

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overall survival compared to chemotherapy (HR 0.51, 95% CI 0.41-0.62) in previously treated individuals.[44,47] Additionally, immunotherapy with pembrolizumab plus chemotherapy improves progression-free survival (HR 0.65, 95% CI 0.49-0.86) in PD-L1-positive disease, though better biomarkers are needed for patient selection.[36]

Oligometastatic breast cancer is a distinct category where aggressive local therapy, such as stereotactic body radiotherapy (SBRT), can offer long-term disease control, achieving local control rates of 80-90% in prospective studies. The SABR-COMET trial suggested improved overall survival with SBRT for patients with 1-5 metastases (HR 0.57, 95% CI 0.30-1.10), although breast cancer-specific data remain limited.[45] Brain metastases pose a significant challenge, with emerging strategies including HER2-targeted tyrosine kinase inhibitors with CNS penetration (tucatinib, neratinib), antibody-drug conjugates (trastuzumab deruxtecan), and immunotherapy showing promise.[43]

DISCUSSION

Interpretation of Findings

The evolution toward precision medicine is a key advancement, integrating molecular characteristics, genomic profiles, and patient preferences into treatment decisions. Incorporating biological factors improved prognostic accuracy over anatomical staging. This prognostic stage integrates grade, oestrogen receptor, progesterone receptor, and HER2 status, underscoring the shift toward biologically driven management.[15] The represents a paradigm shift from historical approaches requiring 1-2 cm margins, reducing re-excision rates and improving cosmetic outcomes without compromising oncological safety. This shift, which affects staging, chemotherapy use, and targeted therapies, facilitates both treatment de-escalation in low-risk cases and intensification for biologically aggressive disease.[46] The goal is to minimize unnecessary toxicity while ensuring optimal oncologic outcomes, shortening treatment, and reducing patient visits. Practical examples include omitting axillary dissection in limited nodal disease, utilizing partial-breast irradiation, and employing genomic assays to guide the need for chemotherapy. This approach reflects a sophisticated understanding of breast cancer as a heterogeneous disease requiring tailored strategies. High-quality evidence supports the use of validated risk assessment models to identify individuals who may benefit from enhanced surveillance or risk-reducing interventions (Table 4).

Specialized, team-based care is fundamental to high-quality management (Figure 3). Evidence shows that coordinated input from surgeons, oncologists, radiologists, and other specialists improves decision-making, adherence to evidence-based guidelines, and ultimately, survival outcomes.[36] While consistent with prior reviews, this current analysis offers a more comprehensive integration across the entire continuum of care. Earlier reports often focused narrowly on specific areas,[5] such as surgical margins or adjuvant chemotherapy selection (Denduluri et al., 2018).[7] This review, however, contextualizes individual treatment choices within the broader therapeutic landscape, highlighting the interactions among imaging, surgery, radiotherapy, and systemic options. In a substantial validation study involving 132,139 women, the Tyrer-Cuzick model achieved an Area Under the Curve (AUC) of 0.70 (95% CI: 0.68–0.72). This result is regarded as acceptable in the context of medical modelling, suggesting that the model demonstrates a fairly good capacity to distinguish between high-risk and low-risk women, and possesses statistical power.[11,12]

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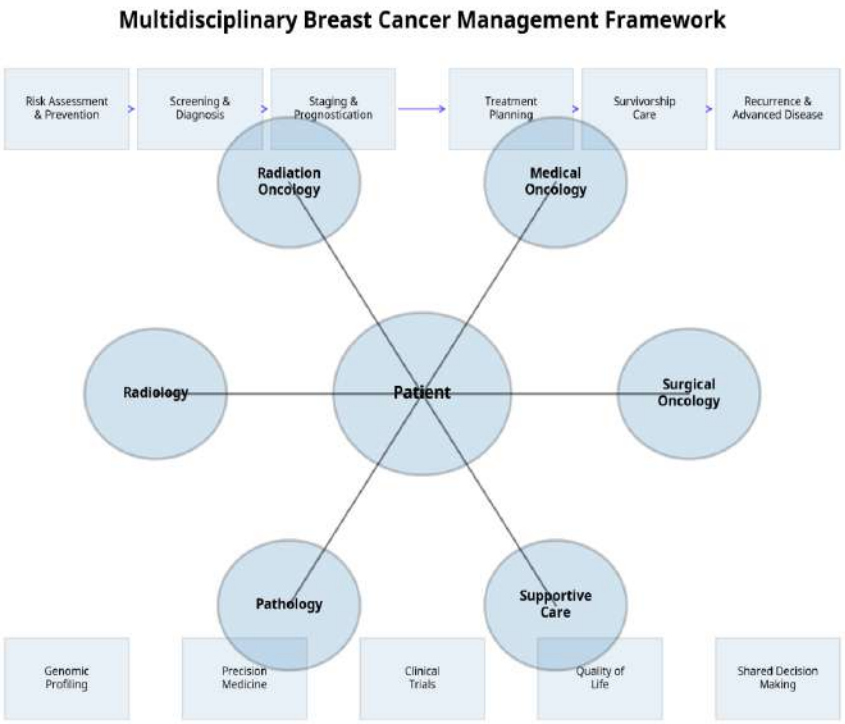

Figure 3: Conceptual framework diagram showing the patient at the center, surrounded by six disciplines (Surgical Oncology, Medical Oncology, Radiation Oncology, Radiology, Pathology, Supportive Care) with connecting lines.

Notable findings include the rapid emergence of evidence supporting novel approaches such as abbreviated MRI protocols, ultra-hypofractionated radiotherapy, and the use of immunotherapy in early triple-negative disease. These developments underscore the dynamic nature of the field and the necessity for regular evidence updates. The approach of using comprehensive geriatric assessment, utilizing validated tools (G8, VES-13) detects vulnerabilities impacting treatment tolerance, enabling tailored interventions. The decision algorithm presented in Figure 4 provides a practical framework for integrating these advances into clinical practice, recognizing that optimal management must consider both disease and patient-specific factors.

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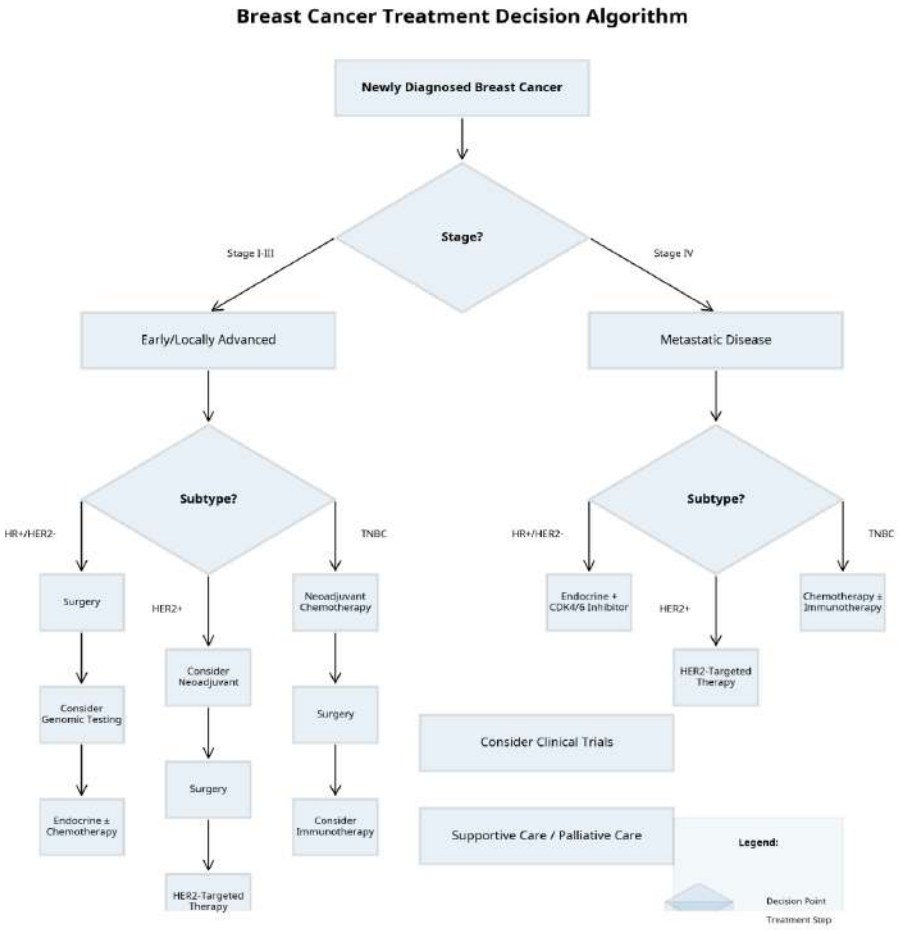

Figure 4: Flowchart showing treatment decision pathways based on stage (I-III vs. IV) and molecular subtype (HR+/HER2-, HER2+, TNBC). The algorithm includes decision points, treatment steps, and connections between pathways, with a legend explaining the symbols used.

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Review's Limitations

While comprehensive, the review has some limitations:

1.Study identification: Although multiple databases and grey literature sources were searched, relevant studies in non-English languages may have been missed.

2.Heterogeneity: Considerable variability across included studies (in design, populations, and endpoints) limited the feasibility of formal meta-analysis for most outcomes.

3.Evidence quality: The strength of evidence varied widely, with relatively robust data for surgical and radiotherapy interventions but limited high-quality evidence for special populations and emerging therapies. Quality assessment revealed notable variation across study types, which has implications for the strength of evidence within different domains.

4.Scope: Our focus was primarily on clinical management. Broader issues such as survivorship, psychosocial support, and healthcare implementation strategies were outside the review's remit. Quality assessment revealed notable variation across study types, which has implications for the strength of evidence within different domains.

5.Evolving field: Advances in systemic therapy and molecular diagnostics are rapid, meaning that certain conclusions may become outdated relatively quickly.

Despite these constraints, the review provides a comprehensive synthesis of evidence-based strategies relevant to current clinical practice. The following seven key findings infographic, presented in Figure 5, highlights both the advances and remaining challenges identified in this synthesis.

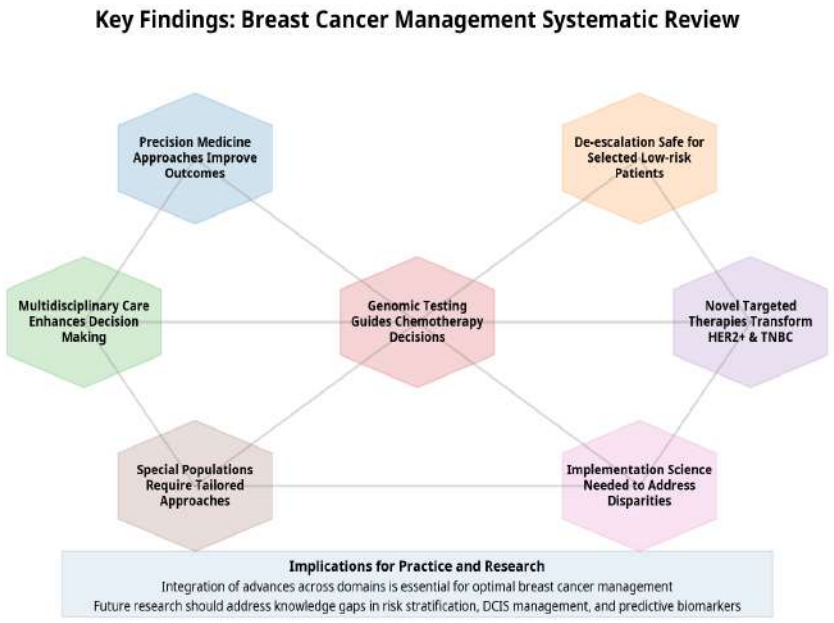

Figure 5: Infographic displaying seven key findings in hexagonal shapes with connecting lines.

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Implications for Practice and Policy

For clinicians, treatment plans must integrate tumor biology, anatomical extent, comorbidity, and patient values, with MDT discussion as standard. De-escalation is appropriate for selected low-risk patients (e.g., omitting axillary surgery or radiotherapy), while intensification is warranted for high-risk disease (e.g., targeted therapies in HER2-positive or BRCA-mutated cancers). Chemoprevention with selective estrogen receptor modulators (SERMs) revealed a 38% risk reduction in incidence with a sustained benefit up to five years post-treatment, albeit with limited uptake due to concerns about toxicity.[13] Comprehensive geriatric evaluation optimizes decisions for older adults. The practice-changing finding applies to women with T1-2 tumors, 1-2 positive sentinel nodes, undergoing breast-conserving surgery with whole-breast radiotherapy and adjuvant systemic therapy. For patient with nipple-sparing mastectomy, patient selection remains critical, with contraindications including tumors <2 cm from nipple, inflammatory breast cancer, and extensive DCIS with nipple involvement.[26] For policymakers, the review highlights the need for equitable access to genomic testing, advanced imaging, and multidisciplinary care, requiring resource-stratified guidelines and implementation science to bridge evidence to real-world practice.

Future Research Directions

There are still several topics that need more research:

-Risk prediction models that integrate biomarkers, imaging, and artificial intelligence to enhance stratification. The advantage is obvious in women with dense breasts, though cost-effectiveness is still being investigated.

-Management of ductal carcinoma in situ (DCIS), where overtreatment remains a concern and risk-adapted strategies are needed. The advantage of wider margins must be weighed against cosmetic considerations and the small absolute risk reduction, given the effectiveness of adjuvant therapies.[22]

-Novel predictive biomarkers for therapy selection, especially in metastatic disease with multiple available options.

-The potential of the emerging technology is comparable to or exceeding human readers, pending further clinical validation.[19]

-Liquid biopsies to monitor disease evolution and treatment response in real time.

-Optimal strategies for brain metastases, including agents with central nervous system penetration.

-Implementation research to close the evidence-to-practice gap, particularly in resource-constrained environments.

CONCLUSION

Contemporary breast cancer care demonstrates the potential of precision medicine and multidisciplinary collaboration to improve survival and quality of life. Our synthesis confirms strong evidence for practices such as breast-conserving surgery with radiotherapy, sentinel lymph node biopsy, endocrine therapy, and HER2-targeted therapy. Moderate-level support exists for approaches including hypofractionated radiotherapy, selective omission of axillary dissection, and the use of genomic assays to avoid unnecessary chemotherapy.

Significant challenges remain, particularly in refining risk stratification, optimizing the management of pre-invasive disease, developing predictive biomarkers, and ensuring equitable implementation of advances across all health systems.

Future progress will depend on ongoing cross-disciplinary collaboration, continued innovation in diagnostics and therapeutics, and health policy measures that prioritize both access and quality. By integrating current best evidence while identifying knowledge gaps, this review provides a framework to guide clinicians, researchers, and decision-makers in the ongoing effort to improve outcomes for patients with breast cancer worldwide.

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The authors declare no conflicts of interest related to the content of this review.

Author Contributions:

Contributions were documented in line with the **CRediT taxonomy:**

-Conceptualization & methodology: N.J.S. Elsaadi, T.F. Houni, A.M. Amaari

-Data acquisition & validation: M.O. Al-Jahany, M.A. Moftah

-Analysis & interpretation: All authors, N. E. Azouz

-Manuscript drafting: N.J.S. Elsaadi, T.F. Houni, A.M. Obaeid

-Critical revisions & final approval: All authors

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Supplementary Materials:

Primary search terms included:

"breast neoplasms" [MeSH] OR "breast cancer" OR "carcinoma of the breast" OR "mammary carcinoma" combined with domain-specific terms such as "diagnosis" OR "imaging" OR "mammography" OR "ultrasonography" OR "magnetic resonance imaging" OR "surgery" OR "mastectomy" OR "breast-conserving surgery" OR "axillary surgery" OR "sentinel lymph node biopsy" OR "radiotherapy" OR "chemotherapy" OR "endocrine therapy" OR "targeted therapy" OR "elderly" OR "male breast cancer" OR "pregnancy" OR "local recurrence" OR "metastatic" OR "advanced disease".

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Extra uterine growth restriction and its related factors in extremely and very low birth weight babies including 1500 grams admitted to Jammhoria hospital in Benghazi.

Aziza I.Kadwar [1*], khadiga I. Shreef [1], Isaaida A. Alsaeiti [2], Nadia AM. Aldarogi [3]

Original Research Article

Abstract

Background:Extra-uterine growth restriction (EUGR) in premature infants remains a major challenge for neonatologists worldwide. In the neonatal intensive care unit (NICU), suboptimal nutrition and the fear of advancing feeds are key contributors. Updated feeding protocols that support rapid but safe feeding advancement, breast milk fortification, and close monitoring of growth parameters are essential to achieving optimal nutritional outcomes and preventing long-term neurodevelopmental impairment.

Objective: To determine the frequency of extra-uterine growth restriction (EUGR) among premature infants in Benghazi and identify associated risk factors.

Method: This cross-sectional study was conducted in Benghazi. Medical records of 107 premature infants were obtained from the neonatal clinic. All preterm infants born at <34 weeks' gestation and weighing ≤1500 grams were included. Growth measurements at birth, discharge, and 40 weeks corrected age were plotted on Fenton growth charts. Weight <10th percentile was classified as EUGR. A p-value <0.05 was considered statistically significant.

Results: EUGR was identified in 85 infants (79%) at discharge and in 63 infants (58.8%) at 40 weeks corrected age. Significant risk factors for EUGR at discharge and at 40 weeks included lower birth weight (p = 0.01; p = 0.005), longer hospital stay (p = 0.007; p = 0.01), small for gestational age (SGA) (p = 0.000; p = 0.02), and sepsis (p = 0.03; p = 0.001). Additionally, gestational age 33–34 weeks (p = 0.001) and multiple births (p = 0.03) were significant risk factors for EUGR at discharge only.

Conclusion: Extra-uterine growth restriction is highly prevalent among Libyan premature infants. Lower birth weight, prolonged hospitalization, SGA status, gestational age of 33–34 weeks, and multiple births were significant associated risk factors.

Recommendations: Implementation of updated feeding protocols for premature infants in Libya—including rapid but safe advancement of enteral feeds, breast milk fortification, and close monitoring of growth parameters—is essential to improving nutritional outcomes and reducing the risk of EUGR.

Keywords: Benghazi, extra-uterine growth restriction, extremely low birth weight, very low birth weight, premature infants.

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INTRODUCTION

The survival rate of extremely and very low birth weight infants has improved significantly in recent years, largely due to advances in neonatal medical care, including enhanced respiratory and nutritional support (1,2). However, suboptimal nutrition remains a major challenge in many Neonatal Intensive Care Units (NICUs) worldwide, often leading to extra-uterine growth restriction (EUGR) among premature infants.

EUGR is defined as weight, head circumference, or length ≤10th percentile of intrauterine growth expectations, assessed at discharge, 36 weeks, or 40 weeks corrected age (3). Major neonatal societies—including the American Academy of Pediatrics, the Canadian Pediatric Society, and the European Society for Pediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN)—recommend that postnatal growth in preterm infants should approximate intrauterine growth rates, ensuring that growth at corrected age is comparable to that of term infants.

A number of factors contribute to this largely irreversible condition. Suboptimal early nutrition, particularly inadequate protein intake in the first weeks of life, is considered one of the most important contributors (4). Other independent risk factors associated with EUGR include intrauterine growth restriction (IUGR), need for assisted ventilation on the first day of life, prolonged respiratory support for more than 28 days, male sex, extended hospitalization, development of bronchopulmonary dysplasia (BPD), necrotizing enterocolitis (NEC), sepsis, exposure to steroids during hospitalization, delayed return to birth weight, and delayed achievement of full enteral feeds (3,5–7).

Over the last 10–15 years, nutritional guidelines have been refined to reduce the risk of EUGR, and these updates have shown promising outcomes. Current recommendations support early and aggressive initiation of both parenteral and enteral nutrition, with progressive advancement to full enteral feeds (8–11). These approaches have been associated with earlier recovery of birth weight, improved weight at discharge, shorter duration of parenteral nutrition, earlier attainment of full feeds (8,11), lower rates of late-onset sepsis, and reduced incidence of NEC (9,12). Furthermore, milk fortification—whether human milk fortifiers or preterm formulas—along with post-discharge nutritional support provides an opportunity for catch-up growth (13).

Recent findings demonstrate that fortification of breast milk, close monitoring of growth parameters, and adherence to consensus guidelines from major neonatal societies can enable preterm infants to achieve growth trajectories that align with their birth percentiles. ESPGHAN has also introduced updated recommendations for targeted nutrition during critical illness, emphasizing optimal protein and energy delivery to support appropriate growth (14). In Japan, breast milk fortification standards were enhanced in the 2010s, and updated enteral feeding guidelines were introduced in 2017 (15).

EUGR is associated with poor neurodevelopmental outcomes, with long-term and often irreversible consequences (16,17). With the advancement of digital technologies, machine learning (ML) and artificial intelligence (AI) have been applied to better understand factors influencing EUGR. For example, Bozzetti et al. used ML to identify clinical and nutritional predictors of EUGR among infants born before 33 weeks and demonstrated the strong predictive value of early clinical and nutritional variables (18).

In Libya, the absence of standardized feeding guidelines—combined with reluctance among some clinicians to initiate early and aggressive feeding in extremely low and very low birth weight or critically ill infants—contributes to a higher risk of EUGR. Although national nutritional strategies were launched in 2020, implementation remains challenging, particularly in the care of sick premature infants. This study aims to highlight the magnitude of this problem in Benghazi and to raise awareness of the need for urgent improvements in nutritional practices for premature infants.

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AIM of THE STUDY

-To estimate the frequency of extra-uterine growth restriction (EUGR) at discharge and at 40 weeks corrected age among extremely and very low birth weight premature infants (≤1500 grams).

-To identify the clinical characteristics and postnatal factors significantly associated with EUGR in premature infants ≤1500 grams.

METHODOLOGY

It is a cross-sectional study that included 107 premature babies who were discharged from the NICU (neonatal intensive care unit) in Jammhoria Hospital in Benghazi. It is a public maternity hospital where extremely low, very low, and low birth weights (≤ 1500 grams) were born in Benghazi. We selected 107 premature babies who were attending the neonatal clinic for follow-up and for their growth assessment, with inclusion criteria that included premature babies ≤ 34 weeks gestation with birth weight ≤ 1500 grams, and excluded premature babies with congenital anomalies and those babies without recorded data for weight and head circumference at both discharge and corrected age. We collected their files selectively from the neonatal clinic according to inclusion criteria during the period from 2004 until 2015. We collected the data from the files, which include their weight and head circumference at birth, weight at discharge, and at 40 weeks corrected age; their gestational age; sex; duration of hospital stay; and type of pregnancy (single or multiple births). The related factors that may predispose to EUGR were also registered, including the use of a ventilator or bubble non-invasive continuous positive pressure (CPAP), a history of hyaline membrane disease (HMD), necrotizing enterocolitis, a history of apnea, sepsis, bronchopulmonary dysplasia (BPD), and a maternal history of hypertension or preeclampsia. The measurements of birth weight were plotted on the Fenton chart; according to that, we divided them into 2 groups: group of average gestational age (AGA) for those with birth weight > 10th centile, another group of small for gestational age (SGA) with birth weight ≤ 10th centile, and then the weight at discharge and at 40 weeks corrected age were again plotted on charts. Those babies with weight at discharge and 40 weeks corrected age ≤ 10th were defined as babies with extra-uterine growth restriction (EUGR). The two groups of AGA and SGA were compared for the frequency of EUGR, and both groups of EUGR and non-EUGR at discharge and 40 weeks were compared with certain factors that may predispose to EUGR that involved:

Clinical characteristics included sex, birth weight, gestational age, weight for gestational age (either SGA or AGA), duration of hospital stay, and type of pregnancy. Postnatal factors included use of a ventilator or CPAP, a history of hyaline membrane disease (HMD), necrotizing enterocolitis (NEC), a history of apnea, sepsis, BPD, and a history of maternal hypertension or preeclampsia.

DATA ANALYSIS

The preterm infants were categorized into two groups: extra-uterine growth restriction (EUGR) and non-extra uterine growth restriction (non-EUGR). Quantitative data were summarized using descriptive statistics, including mean (M), median (Mdn), and standard deviation (SD). To assess the associations between variables and EUGR status at discharge and 40 weeks corrected age, inferential statistical tests were employed. Categorical variables were analyzed using the chi-square test (χ^2) or Fisher's exact test, as appropriate, while continuous variables were evaluated using the independent samples t-test. A two-sided significance level of $\alpha = 0.05$ was adopted, with p-values < 0.05 deemed statistically significant. All statistical analyses were performed using IBM SPSS Statistics, Version 23 (19).

ETHICAL CONSIDERATIONS

Verbal approval to conduct the study was obtained under the supervision of the Neonatal Department and the neonatal follow-up clinic

RESULTS

In the study, 107 premature babies between the period of 2004 and 2015 whose gestational age was 34 weeks or less with a birth weight of ≤ 1500 grams. Out of them, 73 (68.2%) were female, and the ges-

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tational age between 28 and 32 weeks was estimated in 67.2%; the minimum gestational age was 28 weeks. The mean head circumferences at birth, at discharge, and at 40 weeks were 27.8±1.7, 28±1.39, and 33.59±2, respectively. The birth weight for most of them (63.6%) was between 1200 and 1500 grams; the minimum birth weight was 0.635 kg; the mean birth weight was 1250 grams. (Table 1) (Figure. 1).

Table (1): Descriptive statistics of clinical characteristics for premature babies

Characteristics of study participants	Descriptive statistics				
	Mean	Standard deviation	Median	Minimum	Maximum
Gestational Age in weeks	31.53	1.61	31	28	34
Duration of stay at hospital in days	14.4	9.90	11	1	55
Birth Weight in kg	1.25	0.168	1.28	0.635	1.5
Weight at discharge in kg	1.23	0.885	1.24	0.885	1.600
Weight at corrected age in kg	2.63	0.682	2.6	1.070	4.100
Head circumference at birth in cm	27.81	1.71	28	21.8	33
Head circumference at corrected age in cm	33.59	2.019	34	29	39

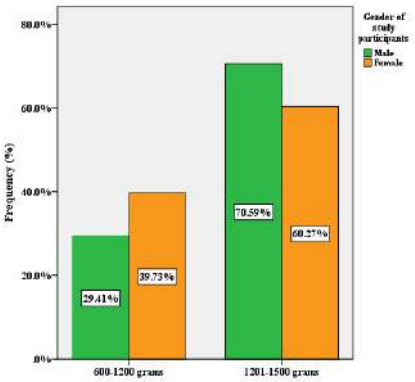

Figure.1: Distribution of premature babies by their birth weight.

The duration of stay at the hospital for 79.4% of premature babies was 1-20 days (Fig. 2). Almost all premature babies (59%) had a birth weight that was average for gestational age (AGA); it means that their birth weight was above the 10th centile. The pregnancy was single in 70.1% (Table 2).

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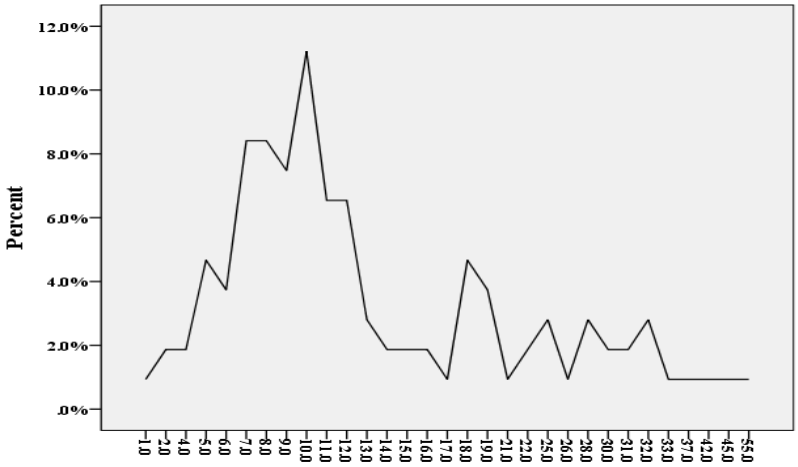

Figure 2: Duration of hospital stay for premature babies

Table (2): Clinical characteristics of extremely and very low birth weight babies ≤ 1.5kg and with ≤ 34 weeks

Clinical characteristics		Frequency	%
Sex	Male	34	31.8
	Female	73	68.2
Gestational weeks	28-30	36	33.6
	31-32	36	33.6
	33-34	35	32.7
Birth weight (kg)	0.600-1.2	39	36.4
	1.201-1.5	68	63.6
Weight for gestational age	SGA	44	41.1
	AGA	63	58.9
Duration of hospital stay (days)	1-20	85	79.4
	21-60	22	20.6
Type of pregnancy	Single	75	70.1
	Twin	24	22.4
	Triplets and quadruplets	8	7.4

There were a lot of morbidities that can contribute to extrauterine growth restriction in the study group listed in Table 3, including hyaline membrane disease (HMD), which was represented in 77.6% of premature infants.

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Table (3): Postnatal factors among premature babies

Clinical characteristics		Frequency	%
HMD Missed 2 cases	Yes	83	77.6
	No	22	20.6
Sepsis	Yes	23	21.5
	No	84	78.5
NEC	Yes	6	5.6
	No	101	94.4
ventilator support	Yes	6	5.6
	No	101	94.4
Bubbling CPAP	Yes	45	42.1
	No	62	57.9
Apnoea	Yes	19	17.8
	No	88	82.2
BPD	Yes	1	0.9
	No	106	99.1
Maternal hypertension Missed 64 cases	Yes	24	22.4
	No	19	17.8

-The estimation of EUGR in our study was at two groups of age: at discharge and 40 weeks corrected age. A total of 85 (79%) of infants had EUGR at discharge (Figure. 3), compared to 63 (58.8%) of premature babies who had EUGR at 40 weeks (Figure. 4).

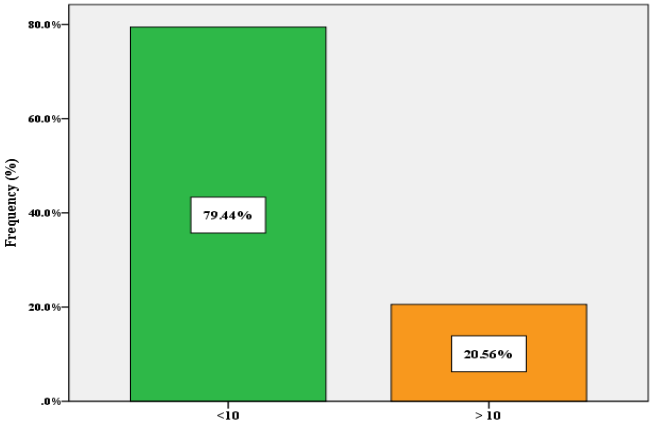

Figure.3: Frequency of EUGR according to weight at discharge

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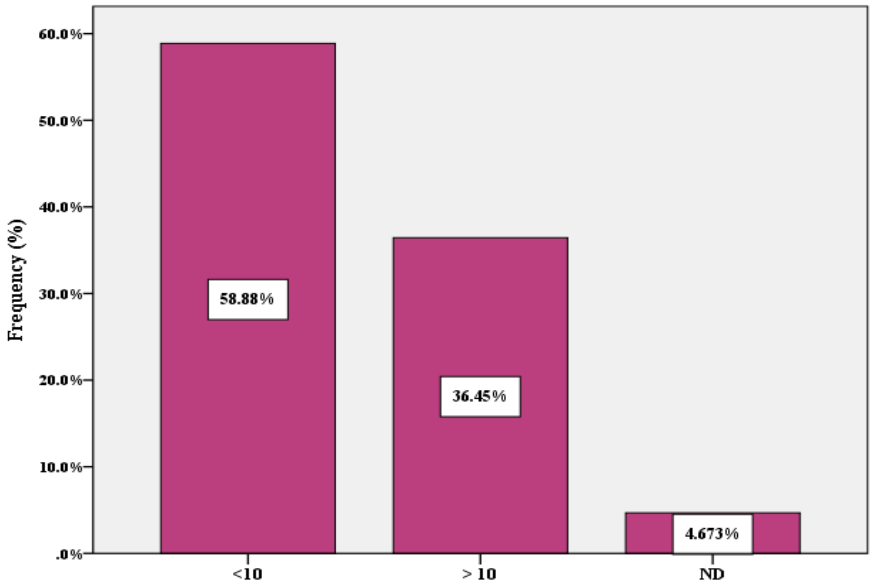

Figure.4: Frequency of EUGR according to weight at 40-week corrected age

Clinical characteristics of EUGR and non-EUGR at discharge: The females were more in the EUGR group (57) than the males, but the sex was negatively correlated to EUGR. Significant differences between EUGR and NON-EUGR groups were identified for the smaller birth weight (SGA) (p=0.000), longer stay in hospital (p=0.007), lower birth weight (p=0.01), premature birth from multiple pregnancy (p=0.03) (whether twin, triplets, or quadruplets), and 33-34 gestational weeks (p=0.001). All were statistically related to EUGR (Table 4).

Table (4): Association between clinical characteristics and EUGR at discharge:

Clinical characteristics		EUGR	No EUGR	X^2	P-value
Sex	Male	28	6	0.259	0.611
	Female	57	16		
Gestational weeks	28-30	23	13	14.823	0.001**
	31-32	27	9		
	33-34	35	0		
Birth weight (kg)	0.600-1.2	36	3	6.222	0.01**
	1.201-1.5	49	19		
Weight for gestational age	SGA	44	0	19.342	0.000**
	AGA	41	22		
Duration of hospital stay(days)	1-20	63	22	7.168	0.007**
	21-60	22	0		
Type of pregnancy	Single	59	16	6.46	0.03**
	Twin	22	2		
	Triplets and quadruplets	4	4		

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The clinical characteristics of EUGR and non-EUGR at 40 weeks: smaller for gestational age (SGA) (p=0.02), lower birth weight (p=0.005), and longer stay in hospital (p=0.01) were significantly associated with EUGR. whereas sex, gestational age, and multiple gestation were negatively correlated to EUGR (Table 5).

Table (5): Association between clinical characteristics and EUGR at 40 weeks corrected ages

Clinical characteristics		EUGR	No EUGR	X^2	P-value
Sex	Male	23	10	1.64	0.439
	Female	40	29		
Gestational weeks	28-30	21	11	5.886	0.208
	31-32	20	15		
	33-34	22	13		
Birth weight	0.600-1.2	31	7	10.77	0.005**
	1.201-1.5	32	32		
Weight for gestational age	SGA	32	12	7.653	0.02**
	AGA	31	27		
Duration of hospital stay	1-20	44	37	9.241	0.01**
	21-60	19	2		
Type of pregnancy	Single	43	4	4.24	0.374
	Twin	17	0		
	Triplets and quadruplets	3	1		

Postnatal risk factors for EUGR at discharge and 40 weeks corrected age: there was a significant association between EUGR and history of sepsis at discharge and at 40 weeks ($X^2 = 4.715$, $p = 0.03$) and ($X^2 = 13.52$, $p = 0.001$), respectively (Table 6) (Table 7).

Table (6): Association between the postnatal risk factors and EUGR at discharge:

Risk factors		EUGR	No EUGR	X^2	P-value
HMD Missed 2 cases	Yes	64	19	0.899	0.343
	No	19	3		
sepsis	Yes	22	1	4.715	0.03**
	No	63	21		
NEC	Yes	5	1	0.059	0.808
	No	80	21		
ventilator support	Yes	6	0	1.645	0.200
	No	79	22		
Bubbling CPAP	Yes	34	11	0.717	0.397
	No	51	11		
Apnoea	Yes	17	2	1.424	0.233
	No	68	20		
BPD	Yes	1	0	0.261	0.609
	No	84	22		
Maternal hypertension Missed 64 cases	Yes	18	6	5.028	0.08
	No	12	7		

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Table (7): Association between the postnatal risk factors and EUGR at 40 weeks corrected ages

Risk factors		EUGR	No EUGR	X^2	P-value
HMD	Yes	50	29	0.270	0.874
	No	12	9		
Sepsis	Yes	21	1	13.52	0.001**
	No	42	38		
NEC	Yes	5	1	1.625	0.444
	No	58	38		
ventilator support	Yes	4	2	0.379	0.827
	No	59	37		
Bubbling CPAP	Yes	30	13	2.026	0.363
	No	33	26		
Apnoea	Yes	14	4	2.380	0.304
	No	49	35		
BPD	Yes	1	0	0.705	0.703
	No	62	39		
Maternal hypertension	Yes	15	8	6.97	0.137

DISCUSSION

Our study evaluated how much the EUGR was a frequent challenge between our premature babies, especially those who were extremely and VLBW babies, and for associated clinical characteristics and morbidities as risk factors for EUGR.

Females were most frequent in the study group of premature babies, most of them with smaller gestational ages of 28-32 weeks. The females and the mean gestational age in our study are exactly the same as those in the study done in Ethiopia by Gidi et al. (20). However, in other studies, the same range of gestational ages and mean birth weights were observed, but in contrast to our study, the males were more involved (16, 21-23). In some other studies, higher birth weights were observed (7, 20, 23). The mean of head circumference at birth, at discharge, and at 40 weeks was the same as mentioned by other studies (16, 24), but differs from measurements mentioned by others (26); the head circumference was smaller, as this study was done in extremely premature babies only, those with weights less than 1000 grams. Hospital stays for most premature babies were long, but to avoid the risk of complications like infection and parental separation, most centers tend to limit the duration of hospital stays. In our situation the bed capacity is one of our limitations in the duration of admission. In the study the majority stayed less than 3 weeks and maybe less, especially those with high gestational age or higher weight, as in some studies (7, 20); in contrast, there were premature babies who stayed for nearly 2 months in the unit; it was because of the development of complications like sepsis, apnea, or failure to gain weight (16, 22, 24, 25).

However, the most common morbidity in the study was respiratory distress syndrome (RDS), as in some studies (23, 24), and another was done in Korea by Lee et al. (25), which is a common risk facing premature babies in the NICU. Now it is becoming less common with the advancement of treatment like manufactured surfactant. Other morbidities have become more prevalent, like sepsis, which was mentioned as the first common morbidity in a study done by Liao et al. (21) and the second in other studies (24). In other studies, other morbidities were reported in large numbers, like hypothermia (20) and retinopathy of prematurity (ROP).

Extra-uterine growth restriction (EUGR) is defined as the growth measurement of weight, length, and

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head circumference below the 10th percentile of expected intrauterine growth at postmenstrual age (PMA) at discharge, 36 weeks, or 40 weeks corrected age. In our study we estimated the EUGR between the study group at discharge and 40 weeks corrected age. The results showed that EUGR was higher at discharge (79.4%) as compared to 40 weeks corrected age, which was 58.9%. This decreasing of EUGR at 40 weeks can be explained because most of the babies at this age were at home, as the premature baby stayed at home under the care of their parents, and with good social parental bonding, usually the chance to accept good weight before reaching 40 weeks is high. On the other hand, during the early days of admission, most premature babies, especially with lower birth weight and lower gestational age, had poor weight gain at discharge, which can be attributed to a lot of challenges they faced during admission, and that was reported in the study done in Spain as compared to studies conducted by others where 77% had EUGR at discharge, and it mentioned that it occurred in the first early period of admission (16). Either EUGR at discharge or at 40 weeks, the frequency is still high, and one of the important issues related to that is the delay in initiation of aggressive feeding, either enteral or parenteral, in most NICUs worldwide (7, 21-24). Some meta-analyses and studies found that EUGR was because the infants were receiving less protein and fewer calories (unaggressive feeding protocol) than that recommended by guidelines from international societies. Another cause is lack of breast milk fortification. Morbidities like BPD, IVH, NEC, and ROP (retinopathy of prematurity) represent other causes of EUGR. This can be overcome by increasing the calories up to 160 kcal/kg/day, protein to 4.5 g/kg/day, glucose up to 12.5 upto12.5g/kg/day, fat to 8 g/kg/day (14).

There were a lot of clinical characteristics that were significantly associated with risk of EUGR as compared to the non-EUGR group for discharge weight; they included birth weight, gestational age, weight for gestational age, duration of hospital stay, and multiple pregnancy. For weight at 40 weeks, birth weight, weight for gestational age, and duration of hospital stay were the factors significantly associated with EUGR, but multiple pregnancy and gestational age weren't. This is in line with a previous study done in Shanghai by Shan et al. that revealed the duration of hospital stay, birth weight, gestational age, and SGA are positively correlated to the development of EUGR in premature babies (7). Another study in Taiwan reported that especially extremely low birth weight had poorer growth outcomes (21). Lower birth weight, SGA, and lower gestational age were mentioned in a lot of studies as risk factors for EUGR (16, 20, 22, 24, 25). Because premature babies, especially those weighing less than 1500 grams, take longer to achieve full demand of feeding, that is why now faster aggressive feeding is recommended to get the target of optimal growth for premature babies for good neurodevelopmental outcome, not only for gaining weight. A study done by Burçin İşcan reported in his study that the EUGR group took longer to achieve total enteral nutrition than the Non-EUGR group (26). However, in our study, females were more frequent in the EUGR group, but the sex was negatively correlated with risk for EUGR both at discharge age and 40 weeks, which also was detected by a lot of studies done in other countries (20, 21, 24).

Regarding postnatal morbidities that occur due to a lot of complications that premature babies face in the NICU because of long hospital stays, which increase the risk of EUGR, sepsis was a significant risk factor for EUGR. actually that was one of the causes that lead to delay in initiation of feeding to premature particularly with extremely birth weight and very low birth weight and that increase the risk of EUGR in NICU, in the study was done by Lee et al 2799 infants was enrolled and conducted from 2013 to 2014 ,sepsis reported as positively correlated risk factor for EUGR in addition to respiratory distress syndrome and broncho-pulmonary dysplasia which both unlike in our study were not revealed significantly effected on EUGR(22) which are still common causes of admission and long stay of hospital for premature , sepsis demonstrated as

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significant factor for EUGR also in line with other researches were done in in china as prospective multi-center ,study in USA and in Turkey (23,24 ,26)

CONCLUSION

Extra-uterine growth restriction is one of the challenges facing the outcome of premature babies that survive, which is not a matter of weight gain but rather its relation to neurodevelopmental outcome for preterm babies who survive. It needs encouragement to start feeding, especially in critically ill infants, for whom a lot of research has proved that the benefits of early initiation of feeding outweigh the harm.

RECOMMENDATIONS

It needs more efforts to support optimal nutrition, rapid aggressive initiation of good nutrition, and avoidance of fear of increased feeding when needed for good neurodevelopmental outcomes. advice for updating the feeding protocol and implementing it in NICUs. With new evidence that enteral feeds have a strong role and are superior to parenteral nutrition, this will support premature nutrition and overcome the unavailability of the parenteral one. We need extended research for the outcome after updating and implementing the feeding protocol.

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Conflict of interest:

We declare that there was no conflict of interest or any financial or nonfinancial support.

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Placenta Accreta Spectrum: Epidemiology, Risk Determinants, and Clinical Consequences in Benghazi Medical Centre -2022.

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Original Research Article

Abstract

Background: Placenta Accreta Spectrum (PAS) is a pregnancy-related disorder characterized by the abnormal adherence of trophoblastic tissue to the uterine myometrium, posing a significant risk of maternal mortality. Key risk factors for PAS include placenta previa and prior cesarean deliveries, which have been rising in frequency.

Aim: to explore the risk factors of PAS, incidence, clinical outcomes of affected patients, and strategies to minimize maternal morbidity and mortality.

Method: prospective cohort study conducted on 60 patients during the year 2022 in Benghazi Medical Centre including all patients labeled as PAS cases, Review of records for all patients using the structured data collection sheet. The total number of deliveries, caesarean deliveries, maternal and perinatal deaths had been registered; patients were followed up till delivery.

Results: Mean age of the studied group was 35.37±5.70, 43.3 % of them were multipara , 56.7% with previous cesarean section three or more times, 71.7% of the studied group with grade III placenta previa, 95.0% experienced some complication, after multivariate analysis C.S 3 times and more is considered risk factor for hysterectomy (p value = 0.03) (OR 6.12, 95% CI (1.15-32.59), there was statistical significant association between CS delivery and length of hospital stay (p value =0.005).

Conclusion: Incidence of placenta accreta increases with advanced age, with multipara and with 3 times and more CS. Placenta previa was coexisting factor in 95% of the cases.

Keywords: Placenta accrete, incidence, Risk factors, complications.

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INTRODUCTION

Placenta accreta is the abnormal invasion of placental trophoblasts into the uterine myometrium and this comprises a spectrum of disorders, based on the degree of myometrial invasion; including placenta accreta, placenta increta, and placenta percreta, and recognized as placenta accreta spectrum disorders [1]. Due to the risk of excessive hemorrhage and difficulty in hemostasis, they are associated with increased maternal morbidity and mortality and an interprofessional team should take care for these patients. The incidence of the condition increases with increasing rate of caesarean deliveries. Anyhow, some other factors are related [2]. The International Federation of Gynecology and Obstetrics (FIGO) introduced a grading system for placenta accreta spectrum (PAS) disorders, replacing the previous terms (placenta accreta, increta, and percreta) [3]. With the rising frequency of cesarean deliveries, the incidence of placenta accreta has surged, increasing from 1 in 30,000 pregnancies in the 1960s to 1 in 533 in the 2000s, and as high as 1 in 272 according to one study [4,5]. The risk of developing placenta accreta is strongly correlated with the number of prior cesarean sections, with an odds ratio exceeding 22 for those with five previous cesareans compared to none [6]. Placental adhesions are thought to be caused by the placenta adhering to a defective site in the decidua. Histological diagnosis of placenta accreta spectrum (PAS) disorders provides definitive confirmation, revealing varying degrees of trophoblast invasion and a higher prevalence of trophoblastic inclusions compared to normal placentation [7]. However, other factors warrant increasing attention as well, including advancing maternal age, fertility treatments, and gynecologic surgery. Defining the full clinical range of this condition may impact preconception patient management and reproductive decision making. In addition, as efforts to reduce hemorrhagic morbidity have shifted to predelivery risk stratification, understanding the full range of accreta risk factors should improve proactive management of this severe condition. [5] Advancements in medical imaging, particularly ultrasound technology, have made it a crucial component of routine antenatal care for most pregnant women [8]. Ultrasonography is now fundamental in assessing the fetus, placenta, umbilical cord, and amniotic fluid. The antenatal diagnosis of placenta accreta is typically made through ultrasound, aiding in management planning [9]. It is important to discuss the consequences or results of having placenta accrete spectrum disorders, both for the mother and the fetus, our research aims to investigate the incidence and determine the risk factors of placenta accrete spectrum disorders and evaluate management and outcomes of cases among deliveries.

METHODS

Study Setting, Design, and Sampling This a prospective cohort study conducted during the year 2022 in department of obstetrics and gynaecology in Benghazi Medical Centre (BMC). Our inclusion criteria encompassed all patients prenatally diagnosed with PAS disorders using ultrasound, Doppler, and magnetic resonance imaging (MRI). We excluded patients with impaired liver or renal function, coagulation disorders, spontaneous intraoperative placental separation, other uterine pathologies requiring hysterectomy, and those who declined participation in the study. Our sample was 60 patients after informed consent Patients were followed up till deliveries, all experiments were conducted according to the relevant guidelines and regulations, and the participants were not exposed to any harm or unintended effects. The study adhered to the ethical principles of the Declaration of Helsinki.

ASSESSMENT MEASURES

-Review of records for all patients using the structured data collection sheet which include:

The total number of deliveries, caesarean deliveries, maternal and perinatal deaths

-Pregnant women were asked about the following:

Age, Parity, Previous abortions, history of infertility, uterine surgery or procedures, detection of PAS (weeks of gestational age), Co-morbidities, coexisting placenta Previa and its degree, Antenatal diagnosis (presence of antenatal bleeding or not) and

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Placenta description: (Accrete, Increta, Percreta)

- Outcomes:

Caesarean delivery Planned (Yes, No), Caesarean delivery (Elective Emergency), Method of placenta removal, Need for blood transfusion (Yes, No), Hysterectomy (Yes, No), Bladder injury: (Yes, No), Hospital stays in days, Critical care admission (Yes, No), Death (Yes, No)

early neonatal death (Yes, No).

ETHICAL CONSIDERATIONS

Confidentiality of data was assured using anonymous form of data collection. No interventions and no other use for data. Legal access for the data through alleged administrative permission.

STATISTICAL ANALYSIS

Data was analyzed using statistical package for social science (SPSS) version 26. Descriptive statistics as frequency and percentage. Inferential statistics were applied when needed Chi-square(X^2), t test and Student t test (or Mann-Whitney U test for non-normally distributed data) to find the difference in the distribution of the variables between the internal comparison groups, P-value was considered significant when ≤ 0.05. Data was presented in form of tables.

RESULTS

Our study includes 60 patients with placenta accreta, age of patients ranges from (20-44) years, with mean age group was 35.37±5.70, 38.3% of the studied group with OMA, 31.7% of the studied group with AMA and 30.0 % VAMA (Table 1).

Our results detected that 43.3 % of the studied group were multipara, 88.3% of studied group with previous abortion, 56.7% of them with previous cesarean section three or more times, 71.7% of the studied group with grade III placenta previa, 96.7% no history of infertility, and 13.3% of them with history of Evacuation and curettage (Table 1).

Regarding other related Comorbidities, we found anemia (11.7%), hypertension (8.3%), bronchial asthma (3.3%), diabetes (3.3%) and Thromboembolic disorders.

The majority of women (95.0%) experienced composite complications, 33.3% of them had hysterectomy, 21.7% of them had critical care admission, 20% with bladder injury (Table, 1).

Table (1): Demographic data and clinical history of the studied cases:

Variable		N	%
Age:	OMA* AMA* VADA*	23 19 18	38.3 31.7 30.0
Parity	Multipara Not multipara	26 34	43.3 56.7
History of abortion	No history of abortion History of ab abortion	7 53	11.7 88.3
Number of CS	One Two Three or more	7 19 34	11.7 31.7 56.7
History of infertility	No history of infertility History of infertility	58 2	96.7 3.3
Myomectomy	-None -Myomectomy	1 59	1.7 98.3
History of Evacuation and curettage	None Once Twice three	52 5 2 1	86.7 8.3 3.3 1.7
Comorbidities and pregnancy complication	Anemia Asthma Thromboembolic Diabetes Hypertension	7 2 1 2 5	11.7 3.3 1.7 3.3 8.3

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Variable		N	%
Obstetric Complication	-Co-existing Placenta Previa -Active Antepartum bleeding -Polyhydramnios -GDM** -PIH**	57 13 2 3 1	95.0 21.7 3.3 5.0 1.7
Grade of Coexisting Placenta Previa	-Grade I -Grade II - Grade III	8 6 43	13.3 10.0 71.7

*OMA: Optimal maternal age, *AMA: Advanced maternal age * VAMA: very advanced maternal age.

**GDM: gestational diabetes, ** PIH: pregnancy induced hypertension

Fifty five percent of the studied sample with Elective Cesarean section, most of our studied group (93.3%) with placenta increta and accrete, 95% with composite maternal complication (Excessive hemorrhage over 1500 ml, relaparotomy, injuries to adjacent viscera and Disseminated Intravascular Coagulation) ,most of sample have no perinatal deaths (85%), only 11.7 % has early neonatal death (Table, 2).

Table (2): Delivery data and Outcome of pregnancy of the studied group:

Variable		N	%
Cesarean section	Planned Unplanned	42 18	70 30.0
Actual setting of Cesarean section	Elective Emergency	33 27	55.0 45.0
Placenta Accrete spectrum	Percreta Other type (increta- Accrete)	4 56	6.7 93.3
Maternal Outcome	-Composite Maternal outcome* -Maternal death -Critical care admission -Bladder Injury -Hysterectomy - Needs for blood transfusion	57 2 13 12 30 57	95.0 3.3 21.7 20.0 33.3 95.0
Perinatal death	-No perinatal death -IUFD** -Early neonatal death	51 2 7	85.0 3.3 11.7

* Composite Maternal outcome (representing maternal morbidity and/or mortality)

**IUFD: intrauterine fetal death

There is statistical significant association between three or more cesarean section and more hysterectomy (p value =0.002) and after multivariate analysis more than 3 times C.S is considered risk factor for hysterectomy (p value = 0.03) OR (6.12, 95% CI (1.15-32.59) , but there was statistically insignificant relation between advanced age and hysterectomy , in addition there was no relation with (multipara, any abortion, any previous procedures, any Comorbidities, any antepartum bleeding and Grade III PP) (Table,3).

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Table (3): Association of Maternal Factors with Hysterectomy

Factor	Hysterectomy			
	Univariate		Multivariate	
	P value	Odd (CI 95%)	P value	Odds (CI 95%)
AMA	0.133	2.45(0.74-8.05)	-	-
VAMA	0.55	1.42(0.44-4.49)	-	-
Grand multi	0.01*	3.85(1.24-11.9)	0.44	1.23(0.34-4.24)
History of infertility	0.31	1(0.08-11.7)	-	-
Any abortion	0.49	3.35(0.37-29.9)	-	-
Any previous procedure	0.44	1.75(0.41-7.39)	-	-
Previous three CS plus	0.001*	7.6(1.93-30.4)	0.03*	6.12(1.15-32.59)
Any comorbidity	0.69	1.25(0.4-3.93)	-	-
Active ante partum bleeding	0.57	0.52(0.12-2.19)	-	-
Grade III PP	0.83	0.88(0.27-2.88)	-	-
Caesarean delivery Planned	0.23	0.5(0.15-1.57)	-	-

*Statistically significant risk factor

Our results showed that, although univariate analysis revealed a significant association between multiparity and urinary bladder injury (p = 0.01), this association was not confirmed in the multivariate analysis; therefore, multiparity was not considered a risk factor for bladder injury. Additionally, no significant associations were found with advanced age, history of infertility, previous abortions, prior procedures, comorbidities, antepartum bleeding, or Grade III placenta previa (Table 4).

Table (4): Association of Maternal Factors with Urinary bladder injury

Factor	Urinary bladder injury			
	Univariate		Multivariate	
	P value	Odd (CI 95%)	P value	Odds (CI 95%)
AMA	0.34	2.1(0.51-8.9)	-	-
VAMA	0.77	1.21(0.31-4.6)	-	-
Grand multi	0.01*	5.47(1.30-22.9)	0.4	1.23(0.34-4.24)
History of infertility	1	-	-	-
Any abortion	0.98	1.57(0.17-14.4)	-	-
Any previous procedure	0.99	1.17(0.21-6.52)	-	-
Previous three CS plus	0.006*	11.96(1.43-100)	0.083	2.25(0.78- 7.82)
Any comorbidity	0.12	2.69(073-9.86)	-	-
Active ante partum bleeding	0.27	2.16(0.53-8.8)	-	-
Grade III PP	0.72	0.74(0.19-2.89)	-	-
Caesarean delivery Planned	0.74	0.82(0.21-3.18)	-	-

*Statistically significant risk factor

Table (5) shows that, based on the multivariate linear regression analysis, there was a statistically significant association between cesarean section (CS) delivery and length of hospital stay (p = 0.005).

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Table (5): Multivariate linear regression to detect factors related to length of hospital stay

Factor	B	Wald X^2	P
AMA	21.530	2.791	0.095
Caesarean delivery Planned	22.292	8.029	0.005*
Any previous procedure	-12.688	1.767	0.184
Active ante partum bleeding	15.853	3.442	0.064
Age	-0.846	0.593	0.441
Intercept**	36.155	1.112	0.292

*Statistically significant risk factor

**Intercept (pre-existing medical illness, gestational disease like pre-eclampsia and thrombocytopenia)

In addition, there was no obvious risk factors related to composite maternal outcome or perinatal deaths (table, 6)

Table (6): Association of Maternal Factors with composite maternal outcome and feotal deaths

Factor	Composite maternal Outcome		Foetal deaths	
	Univariate		Univariate	
	P value	Odd (CI 95%)	P value	Odds (CI 95%)
AMA	0.55	3.42(0.29- 40.1)	0.07	0.41(0.08-2.07)
VAMA	1.0	-	0.25	0.35(0.03-3.16)
Grand multi	1.0	-	0.27	0.48(0.08- 2.71)
History of infertility	1.0	-	0.28	8.66(0.47-157.1)
Any abortion	1.0	-	1.0	-
Any previous procedure	1.0	-	1.0	-
Previous three CS plus	0.57	2.75(0.23-32.1)	1.0	-
Any comorbidity	1.0	-	1.0	-
Active ante partum bleeding	0.52	0.53(0.04-6.39)	1.0	-
Grade III PP	0.19	5.6(0.47-66.3)	1.0	-
Caesarean delivery Planned	1.0	-	0.11	0.52(0.10-2.63)

DISCUSSION

Placenta accreta spectrum (PAS) disorders have emerged as a major life-threatening obstetric issue, with its incidence rising from 0.12% to 0.31% over the past 30 years and an associated mortality rate of approximately 7.0%. PAS is also linked to significant maternal morbidity, including the need for massive blood transfusions, urinary tract injuries, hysterectomy, ICU admission, sepsis, and prolonged hospital stays.

Our study includes 60 patients with placenta accreta ,age of patients ranges from (20-44) years mean age group was 35.37±5.70, 38.3% of the studied group with Optimal maternal age, 31.7% of the studied group With Advanced maternal age and 30.0 % advanced maternal age, our results in agreement with El Gelany et al.,[10] who found that 32.4 ± 4.2 (23–39) and declared that placenta accreta increase with age more than 32 years , Several authors have agreed on the findings regarding risk factors for PAS disorders. Fitzpatrick et al. [11] identified advanced maternal age as a significant risk factor. Similarly, a 2017 study highlighted that older maternal age, previous cesarean sections, placenta previa, and high parity were independent risk factors for PAS disorders [12]. Other researchers have also reported comparable outcomes [13,14].

Our results detected that 43.3 % of the studied group multipara , 88.3% of studied group with previous abortion , 56.7% of them with previous cesarean section three or more times, 71.7% of the studied group with grade III placenta previa , 96.7% no history of infertility, and 13.3% of them with history of Evacuation and curettage , on the same line El Gelany et al.,[10] It was found that the risk factors for PAS disorders included having two or more previ-

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ous cesarean sections, a parity of three or more, and a prior history of placenta previa. These findings are consistent with those reported by numerous other researchers [11,13].

Numerous previous studies have investigated the risk factors for PAS, primarily focusing on general populations of pregnant women and comparing those with and without the condition. Around half of PAS cases involve a history of one or more cesarean sections and an abnormally positioned placenta, with this combination being identified as a significant risk factor[11,15,16,17,18]. These findings have influenced current clinical practice, leading to PAS screening being focused on women with the combination of previous cesarean sections and an abnormally positioned placenta. However, studies have shown that women with PAS differ in characteristics depending on whether they have this combination of risk factors [18,19]. Therefore, PAS risk factors may be unique to each subgroup and should be studied separately. It is particularly important to maintain a high level of diagnostic suspicion when placenta previa coexists with a history of cesarean delivery. Silver et al.[17] reported that the risk in such cases increases to 40% or more after a third cesarean. In a recent study, one-third of PAS cases involved women with a history of cesarean and placenta previa in the current pregnancy in a study published by Fitzpatrick et al.[11]

Regarding other related Comorbidities, we found iron deficiency anemia (11.7%), hypertension (8.3%), bronchial asthma (3.3%), diabetes (3.3%) and Thromboembolic disorders, other studies by Kloka etal.,[21] The incidence of "anemia during pregnancy" (90.43% vs. 55.18%; $p < 0.001$), "other forms of anemia" (92.34% vs. 38.0%; $p < 0.0001$), and "anemia due to acute bleeding" (91.93% vs. 35.74%; $p < 0.001$) is significantly higher in women with PAS. Given that PAS is often associated with inadequate iron stores, particularly due to peripartum bleeding, effective iron management during pregnancy is essential [22]. National and international Patient Blood Management (PBM) guidelines recommend screening for anemia during the antepartum period and throughout pregnancy whenever anemia is present [23,24].

Majority of women (95.0%) experienced some complication, 33.3% of them do hysterectomy, 21.7% of them had critical care admission, 20% with bladder injury. On the other hand, the study by Birendra et al.,[25] declared that hysterectomy was performed in 87.5% of cases, and similarly, in 91.6% of cases in a study conducted at a tertiary center [26]. Conservative or expectant management should be reserved for carefully selected PAS patients after thorough counseling about the risks, uncertain benefits, and effectiveness [27]. Protocols from the Royal College of Obstetricians and Gynaecologists (RCOG) and the American College of Obstetricians and Gynecologists (ACOG) emphasize the importance of monitoring blood loss, correcting coagulation disorders, and addressing hydro-electrolytic imbalances. Postoperative care in the intensive care unit continues to focus on stabilizing vital signs [26]. In another study, a planned cesarean hysterectomy was performed in 67% of prenatally diagnosed PAS cases, which is considered the preferred treatment approach by experts [28].

Our study declared that 11.7% with neonatal death, 3.3% IUFD and 85% no perinatal mortality, other study by Balayla and Bondarenko [29] who detected that unfavorable outcomes for neonates, according to a comprehensive evaluation of 34 studies.

There is statistical significant association between three or more cesarean section and more hysterectomy (p value =0.002) and after multivariate analysis more than 3 times C.S is considered risk factor for hysterectomy (p value = 0.03) OR (6.12, 95% CI (1.15-32.59) , but there was statistically insignificant relation between advanced maternal age and hysterectomy , in addition there was no relation with (multipara, any abortion, any previous procedures, any Comorbidities, any antepartum bleeding and Grade III PP. On the same line with other studies which declared that multiple cesarean section increased the risk of PAS approximately five- to six-fold (a OR 5.64, 95% CI 3.01–10.57) [30]. Miller et al.'s cohort study demonstrated two to three

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times the risk for PAS in multiple cesarean section (adjusted relative risk 2.96, 95% CI 2.23–3.93) [31], which is an important cause of postpartum uterine atony-related hemorrhage that requires critical care and lead to hysterectomy.

Our results detected that after univariate analysis we found significant association between multipara and Urinary bladder injury (p value =0.01) but after multivariate analysis no association so it is not considered as risk factor for bladder injury, in addition there was no relation with (advanced age, history of infertility, any abortion, any previous procedures, any Comorbidities, any antepartum bleeding and Grade III PP).

Regarding length of hospital stay, we found statistically significant relation between CS delivery and Length of hospital stay (P value = 0.004), also after multivariate analysis, there was statistically significant association between CS delivery and length of hospital stay (p value =0.005).

One potential limitation is the lack of histologic confirmation of PAS in cases where hysterectomy was not performed. However, the prospective study design and the use of predefined criteria reduce the risk of false PAS diagnoses. Another limitation is the small sample size of the studied women. Ideally, we would have preferred to compare these risk factors with a control group of women without placenta accreta.

IN CONCLUSION

Incidence of placenta accreta increases with advanced age, with multipara and with previous three CS plus. Placenta previa was coexisting in 95% of the cases, also associated with antenatal bleeding, outcome of placenta accreta related to some factors as hysterectomy increase among patient with cesarean section more than 3 times. Addressing the growing burden of PAS disorders requires a combination of early detection, appropriate surgical planning,

RECOMMENDATION

-Early detection and diagnosis through routine Screening for High-Risk Women: Women with known risk factors, such as a history of cesarean sections or placenta previa.

- In need further prospective studied to compare these risk factors with another group without placenta accrete and compare outcome between different grade of placenta accrete.

- It is important to do Histologic confirmation of PAS for the cases without hysterectomies

Conflict of interest:

The authors report no conflicts of interest in this work

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Histopathological evaluation of prostate biopsy in-patient with Prostate cancer in Benghazi Medical Center in the period between 2020-2023.

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Aya farag[2], Najah abdalsallam[2], Negeia Rezqallah[2].

Original Research Article

Abstract

This descriptive, cross-sectional study was conducted at Benghazi Medical Center (BMC), Benghazi, Libya. Data were collected from the medical records of 81 patients diagnosed with prostate cancer who were admitted to the oncology department between January 2020 and December 2023. The aim of this study was to describe the demographic, clinical, and histopathological characteristics of prostate cancer patients.

Results: The mean age of the patients was 71.6 years, and 83% of cases occurred among those aged 71–80 years. Overall, 19.8% of patients were smokers. Nine patients (11.1%) had diabetes mellitus, one patient (1.2%) had hypertension, and approximately 84% reported no family history of prostate cancer. Histopathological examination revealed adenocarcinoma in different stages of differentiation, with acinar adenocarcinoma accounting for 95% of cases and ductal adenocarcinoma for 2.5%. Most adenocarcinoma cases presented as Grade I (44.4%), followed by Grades II and IV (17.3% each).

Conclusion: The study demonstrated that most cases occurred in older patients and were diagnosed at an early stage. Acinar adenocarcinoma was the predominant histopathological type, and the low rate of metastasis suggests a favorable prognosis.

Keywords: prostate cancer, adenocarcinoma, PSA, Libyan males, Benghazi, histopathology.

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INTRODUCTION

Prostate cancer is one of the most common malignancies among men, particularly those older than 50 years, and remains a leading cause of cancer-related mortality in industrialized countries (1). Its incidence and outcomes are influenced by a combination of hereditary, environmental, and sociocultural factors, which contribute to the variations observed across populations (2). Genetic predisposition is among the most important determinants of risk, with family history consistently identified as a significant predictor. Evidence from epidemiologic and twin studies confirms the substantial contribution of inherited traits to prostate cancer susceptibility (3). Mutational alterations in genes involved in androgen synthesis and metabolism further support the critical biological role of androgens in carcinogenesis (4,5).

Although some prostate tumors remain latent for years, progression to advanced or metastatic disease significantly increases morbidity and mortality. Understanding the molecular mechanisms underlying this transition is therefore crucial for guiding treatment and improving survival rates. Spondin 3 (RSPO3), previously associated with colorectal and lung cancers, has been proposed as a potential yet underexplored biomarker in prostate cancer (6).

The diagnostic process typically begins with abnormal prostate-specific antigen (PSA) results or suspicious findings on digital rectal examination, followed by histopathological confirmation through biopsy. Management strategies vary according to stage and may include active surveillance, surgery, radiotherapy, or hormonal therapy. In recurrent or advanced cases, androgen deprivation therapy (ADT), chemotherapy, and targeted agents are widely used, with combination regimens often achieving better outcomes (7).

Histologically, prostate adenocarcinoma is the most common type of malignancy, with acinar adenocarcinoma being the predominant subtype. Ductal adenocarcinoma, although less common, is more aggressive. Other rare forms include urothelial carcinoma of prostatic origin and squamous cell carcinoma, both associated with poorer prognoses (8). Accurate histological classification is essential for guiding treatment decisions. Staging relies on several prognostic indicators—including the Gleason grading system, TNM classification, PSA levels, and the Grade Group system—all of which play key roles in determining disease severity and therapeutic strategies (9). This study was aimed to describe the demographic, clinical, and histopathological characteristics of prostate cancer patients.

MATERIALS AND METHODS

This descriptive, cross-sectional study was conducted at Benghazi Medical Center (BMC), Benghazi, Libya. Data were collected from the medical records of 81 patients diagnosed with prostate cancer who were admitted to the oncology department between January 2020 and December 2023. The variables extracted included socio-demographic characteristics, medical history, smoking status, histopathological type, and prostate-specific antigen (PSA) levels.

STATISTICAL ANALYSIS

Data were analyzed using the Statistical Package for the Social Sciences (SPSS). Frequencies, percentages, and mean ± standard deviation (SD) were calculated. Fisher's exact test was used to assess statistical associations. A p-value < 0.05 was considered statistically significant. Figures were generated using Microsoft Excel 2010

RESULTS

During the study period, a total number of 81 cases of prostate cancer were found, patients' age was between 52 to 92 and the mean age was 71.6 years and the majority were between 71 and 80 years as shown in figure 1.

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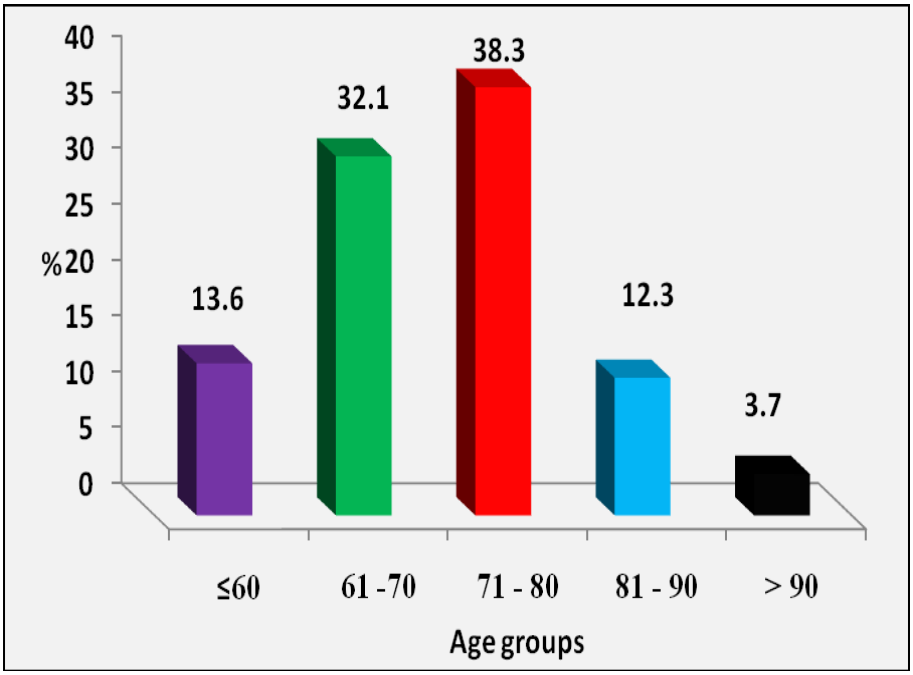

Figure 1. Distribution of patients according to age

As shown in Table 1, the majority of cases (n = 52, 64.2%) were from Benghazi, while 29 patients (35.8%) were from outside the city.

Table 1: Distribution of patients according to place of residence

Address	No.	%
Benghazi	52	64.2
Outside Benghazi	29	35.8
Total	81	100

Figure 2 shows that most prostate cancer patients were nonsmokers (n = 62, 80.2%). Among the patients, 11.1% had diabetes mellitus, 1.2% had hypertension, and 66.7% had both conditions. Additionally, 84% of the cases had no family history of prostate cancer.

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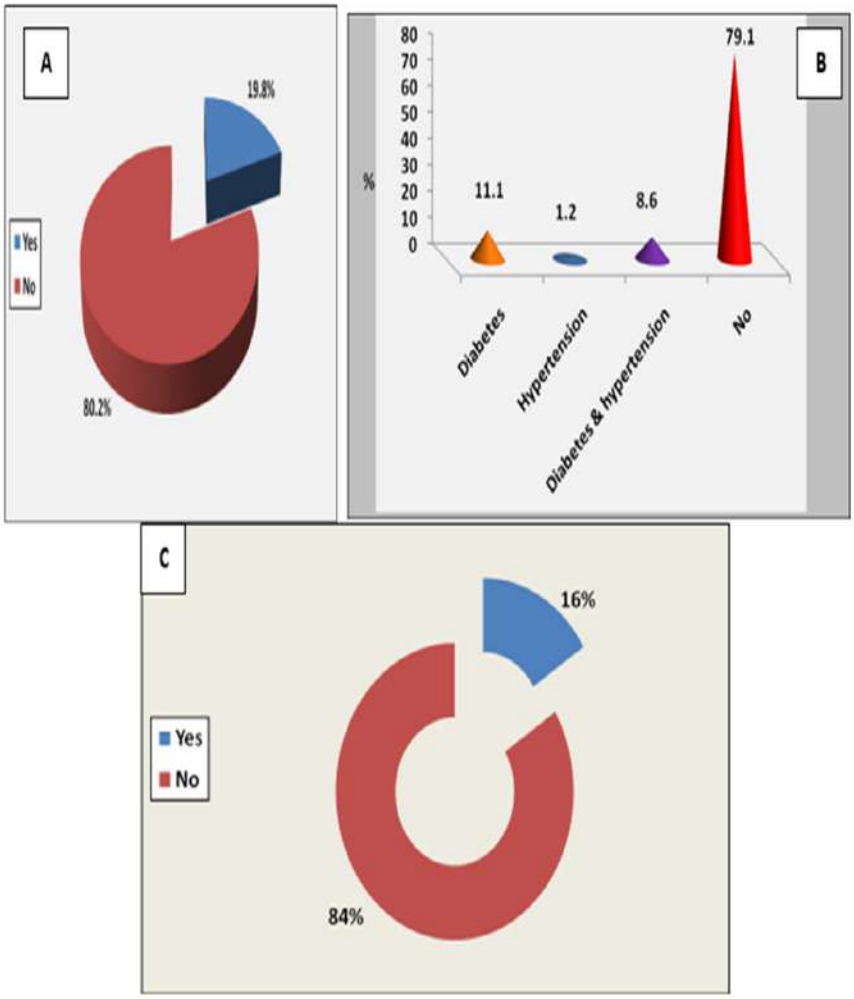

Figure 2. Distribution patients according to smoking status(A), medical history(B), and family history of prostate cancer(C)

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Table 2 shows that the majority of prostate cancer cases were acinar adenocarcinoma (n = 77, 95%), followed by ductal adenocarcinoma (n = 2, 2.5%). Another 2 cases (2.5%) had no recorded histopathological type.

Table 2. Distribution of patients according to the histopathological pattern of prostate cancer

Type of the tumor	No.	%
Acinar Adenocarcinoma	77	95
Ductal Adenocarcinoma	2	2.5
Not recorded	2	2.5
Total	81	100

Figure 3 illustrates the PSA levels at the time of initial presentation. Elevated PSA levels were observed in 29.6% of patients, while 23.5% had normal levels. In approximately 46.9% of the cases, PSA levels were not recorded.

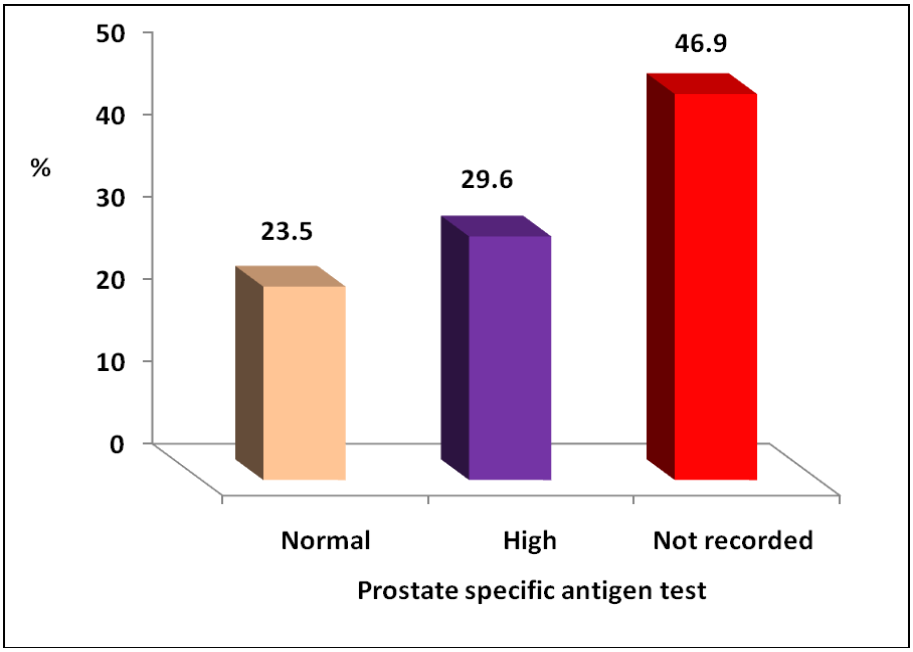

Figure 3. Distribution of patients according to PSA level

According to Gleason Score Grades, figure 4 shows that 36 patients (44.4%) had Grade I disease. Equal proportions of patients (17.3% each) were classified as Grade II and Grade IV, while 14.8% had Grade V.

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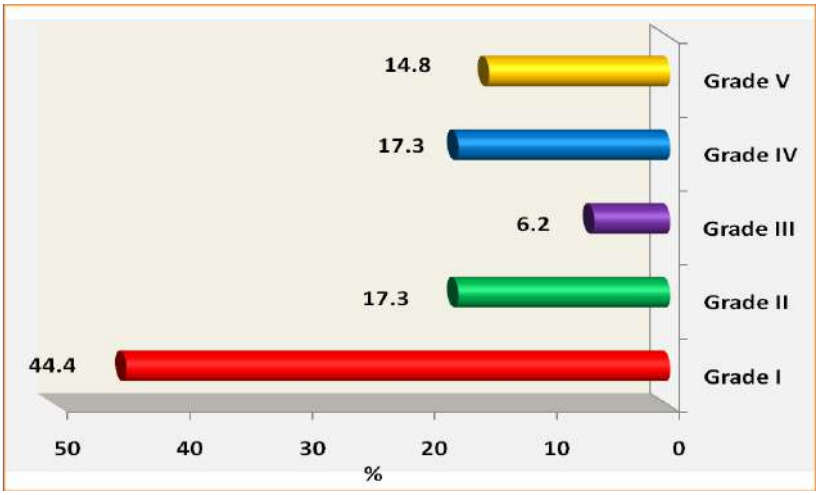

Figure 4. Distribution of patients according to the grade of the prostatic cancer

Figure 5 indicates that only 7 patients had metastatic disease.

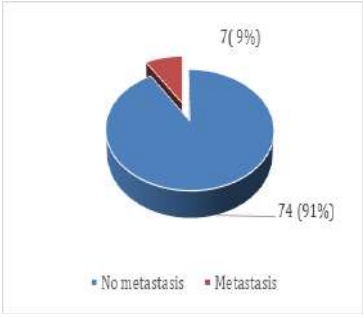

Figure 5: Distribution of the patients according to the disease metastasis.

DISCUSSION

Prostatic diseases—including inflammation, benign prostatic hyperplasia, and carcinoma—are major contributors to male morbidity and mortality. Both benign prostatic hyperplasia and prostate cancer become increasingly common with advancing age (10).

In the present study, 81 patients were included, with ages ranging from 52 to 92 years and a mean age of 71.6 years. Most patients were between 71 and 80 years old. This finding is consistent with a previous study in Benghazi (10), which reported a mean age of 73.1 ± 9.4 years (range 48–90 years), in another study in Benghazi most of the cases were aged 61–70 years (11). This reinforces age as non-modifiable risk factor within our population.

Geographical, environmental, and lifestyle factors play important roles in cancer development (12,13). In this study, most cases originated from Benghazi (64.2%). Although tobacco smoking is widely recognized as a significant risk factor—heavy smokers having a 24–30% higher risk of prostate cancer mortality than nonsmokers (14) 80.2% of the patients in this study were nonsmokers, contrasting with much of the existing literatures. The limited number of patients reporting smoking in our dataset may indicate inaccurate documentation or underreporting rather than the absence of an association.

Family history is another well-established risk factor (15). In this study, only 16% of patients reported a positive family history. The prevalence of diabetes and hypertension among the patients was consistent with previous study (16), which reported similar frequency.

Histopathological evaluation showed that acinar adenocarcinoma was the predominant subtype, in agreement with international classification systems that identify it as the most common prostate cancer subtype (8), followed by ductal adenocarcinoma. Gleason grading revealed that Grade I was the most

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common, followed by Grades II and IV. This is in agreement with a study from Pakistan (17), which also reported Grade I as the most frequent grade, but contrasts with previous findings from Benghazi (10), where Grade IV predominated. These differences may reflect variations in screening practices, patient presentation, or biopsy sampling. Notably, recent recommendations advocate adopting the Grade Group system proposed by Epstein et al. (2016) for improved prognostic accuracy, suggesting a need for standardized grading in future local research (9).

Elevated PSA levels typically reflect the disruption of normal prostate architecture (10). and levels above 20 ng/mL have been strongly correlated with adenocarcinoma (17,18). In this study, 29.6% of patients had elevated PSA values, although incomplete data limited a comprehensive interpretation. PSA is well established as an important diagnostic marker (18). Although PSA screening aims to reduce mortality through early detection, its long-term effect on death rates remains uncertain (19).

Metastasis at presentation occurred in only 8% of cases—significantly lower than the rate reported in other study (20). This comparatively low percentage may indicate improved screening strategies and more timely clinical management in this population.

CONCLUSION

This study found that prostate cancer is predominantly diagnosed among older men in Benghazi, with most cases identified at an early stage of the disease. Acinar adenocarcinoma was the most common histological subtype. The relatively low proportion of metastatic cases at presentation suggests favorable prognostic characteristics within this population.

RECOMMENDATIONS

To improve clinical outcomes, we recommend implementing structured prostate cancer screening programs in Libya, with particular emphasis on high-risk groups. Early detection and timely intervention could substantially reduce disease-related morbidity and mortality.

Multi-center research with standardized methodologies is recommended to establish a more accurate national representation of prostate cancer epidemiology and outcomes.

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We express our sincere appreciation to all individuals who supported the completion of this research. We also extend our gratitude to Benghazi Medical Centre for providing access to the necessary data.

Ethical Statement: This retrospective study was conducted using anonymized patient records from Benghazi Medical Center. No interventions were performed, and confidentiality was strictly maintained in accordance with institutional and international ethical guidelines.

CONFLICT OF INTEREST

The authors declare that there are no conflicts of interest related to this study.

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Prevalence of Skin Findings among Libyan Diabetic Patients.

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Original Research Article

Abstract

Background: Diabetes mellitus (DM) is the most common endocrine disorder. Almost one-third of diabetic patients are affected by cutaneous manifestations during their disease. Cutaneous manifestations of diabetes are caused by either diabetes-induced metabolic changes in the skin or by associated complications like vasculopathy and neuropathy.

Objectives: To estimate the prevalence of skin diseases among patients with diabetes mellitus.

Method: One hundred eighty known adult diabetic patients of either sex attending the outpatient clinic of the diabetic center (Diabetic Center / Benghazi / Libya) for treatment and follow-up of diabetes were randomly selected for the study. Detailed case history of each patient with special attention to cutaneous lesions were taken. A dermatologist performed a detailed dermatological examination.

Results: In this study, most diabetes patients ranged from 41 to 60 years for females, while for males, they were over 60 years. The majority of patients in the current study were females. The most common dermatosis associated with DM was acanthosis nigricans; seen in (69.4%) of patients, skin tag was the second most common dermatosis, accounting for (56.7%) of patients, xerosis was seen in (54.4%), pruritus seen in (37.2%), fungal skin infections found in (25.6%). Diabetic dermopathy was seen in (17.7%), and prayer signs were found in (10.6%). Fifteen (8.3%) diabetic patients had nail changes, and eight (4.4%) diabetic patients had foot ulcers. Diabetic bullae were found in (2.2%); as well as viral infections were seen in (2.2%). Two (1.1%) diabetic patients have bacterial infections.

Conclusion: The prevalence of certain dermatoses was increased among diabetic patients. So, diabetic patients are considered to be at risk of developing certain skin diseases.

Keywords: Diabetes mellitus (DM), Acanthosis nigricans, Skin tag, Xerosis; Pruritus.

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INTRODUCTION

The skin is almost invariably affected by DM; the cutaneous findings of DM are numerous and different studies have reported a different frequency. Most of the patients affected by DM develop skin manifestations eventually (1). Skin findings among patients with DM are attributed to abnormal carbohydrate metabolism, atherosclerosis, microangiopathy, neuron degeneration, impaired host responses, and some other yet undetermined mechanism (2). Various skin disorders associated with diabetes include: acanthosis nigricans, skin tags, diabetic dermopathy, diabetic bullae, diabetic thick skin, yellow skin, eruptive xanthomas, necrobiosis lipoidica, disseminated granuloma annulare, yellow nails, scleredema, diabetic rubeosis, lichen planus and vitiligo (3). Controlling the metabolism of the body may prevent some of these manifestations and also support the treatment (4). Increasing the awareness about skin diseases commonly seen among patients with DM can be associated with a better prognosis of disease through early management (5).

OBJECTIVES

To determine the prevalence of skin diseases among patients with diabetes mellitus.

METHODS

A cross-sectional study was conducted on 180 known adult diabetic patients of either sex attending the outpatient clinic of the diabetic center (Diabetic Center / Benghazi / Libya) for treatment and diabetes follow-up who were randomly selected during the period from January 2022 to March 2022. Non-Libyans, patients with other endocrinal disorders, and pregnant women were excluded from the study group. We also excluded any patients who were not willing to participate. Verbal informed consent was obtained from all participants. Detailed case history of each patient with special attention to cutaneous lesions was taken and dermatologist performed detailed dermatological examination. The data were analyzed by using the statistical package for social sciences program version 18 (SPSS), with a P-value of <0.05 considered statistically significant.

RESULTS

A total of 180 diabetic patients, 43 (23.9%) males and 137 (76.1%) females (Figure 1).

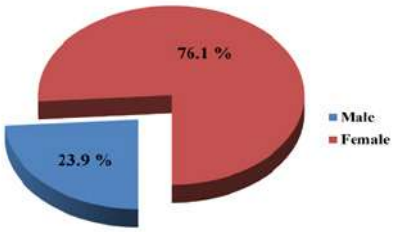

Figure 1. Distribution of patients according to sex.

The most of diabetes patients age group was those over 60 years old followed by 41- 60 years old for males, for females the age group was 41- 60 years followed by those over 60 years old (Table 1).

Table 1. Distribution of patients according to age.

Age group	Female No(%)	Male No(%)	P value
<= 20	1(0.7%)	0(0%)	
40-21	3(2.2%)	2(4,7%)	
60-41	72(52.6%)	16(37.2%)	0.2
=>61	61(44.5%)	25(58.1%)	
Total	137(100%)	43(100%)	

Differences between males and females regarding age groups were not significant (P value = 0.2). The distribution of diabetic patients according to cutaneous findings is shown in Table 2. Acanthosis nigricans was observed in 125 (69.4%) patients; 44% were males and 77.4% were females. The commonest site involved was the neck.

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Table 2. Distribution of diabetic patients according to cutaneous findings.

Cutaneous findings	Female No (%)	Male No (%)	Total No (%)
Acanthosis nigricans	106 (77.4%)	19 (44.2%)	125 (69.4%)
Skin tag	86 (62.8%)	16 (37.2%)	102 (56.7%)
Xerosis	70 (51.1%)	28 (65.1%)	98 (54.4%)
Pruritus	42 (30.7%)	25 (58.1%)	67 (37.2%)
Fungal infections	46 (33.6%)	0 (0%)	46 (25.6%)
Diabetic dermopathy	24 (17.5%)	8 (18.6%)	32 (17.7%)
Prayer sign	18 (13.1%)	1 (2.3%)	19 (10.6%)
Nail changes	8 (5.8%)	7 (16.3%)	15 (8.3%)
Foot ulcer	5 (3.6%)	3 (7%)	8 (4.4%)
Diabetic bullae	3 (2.2%)	1 (2.3%)	4 (2.2%)
Viral infections	4 (2.9%)	0 (0%)	4 (2.2%)
Bacterial infections	0 (0%)	2 (4.7%)	2 (1.1%)

In 80 (52.3%) of cases (Figure 2), the axilla was involved in 60 (39.2%), while the groin was involved in 13 (8.5%). Among 102 (56.7%) patients having skin tags; (37.2%) were males and (62.8%) were females.

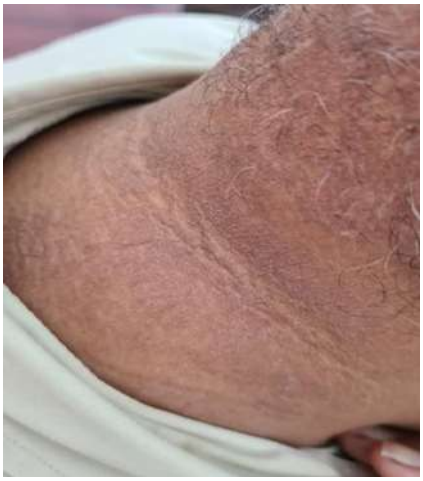

Figure 2: Acanthosis nigricans involving the neck.

The neck alone was involved in 50 (49%) (Figure 3), the neck along with the chest was involved in 42 (41.2%), and the axilla was involved in 10 (9.8%). Xerosis was seen in 98 (54.4%) patients; (65.1%) were males and (51.1%) were females.

Hands were involved in 60 (61.2%) patients (Figure 4), and bodies were involved in 38 (38.8%).

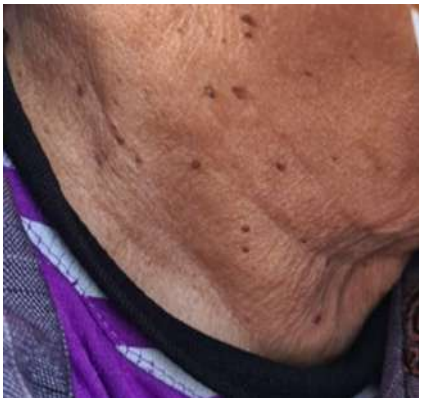

Figure 3. Skin tags involving the neck.

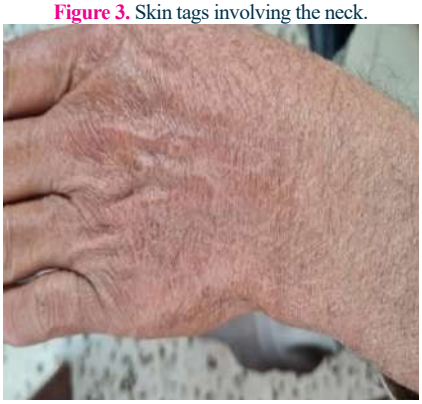

Figure 4. Hand xerosis.

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Pruritus was seen in 67 (37.2%); about (58.1%) was observed in males and (30.7%) was seen in females. Forty-six (25.6%) patients had fungal infections all cases were females (33.6%). Tinea pedis affected about 30 (16.7%) patients (Figure 5), 16 (8.9%) patients had candidiasis, 10 (62.5%) had vaginal candidiasis, and 6 (37.5%) had it under the breast.

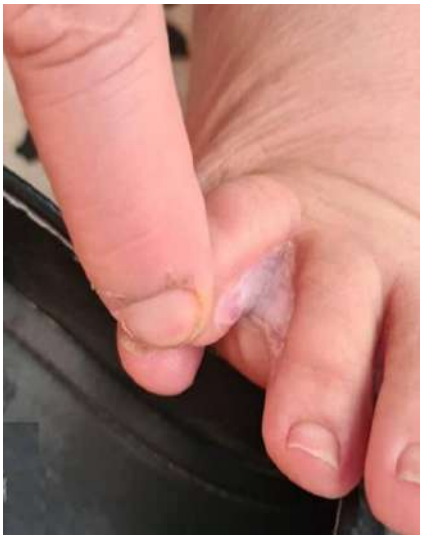

Figure 5: Tinea pedis

Diabetic dermopathy was seen in 32 (17.7%) patients; 18.6% were males and 17.5% were females. Nineteen (10.6%) of diabetic patients had prayer sign; (2.3%) of males and (13.1%) of females (Figure 6).

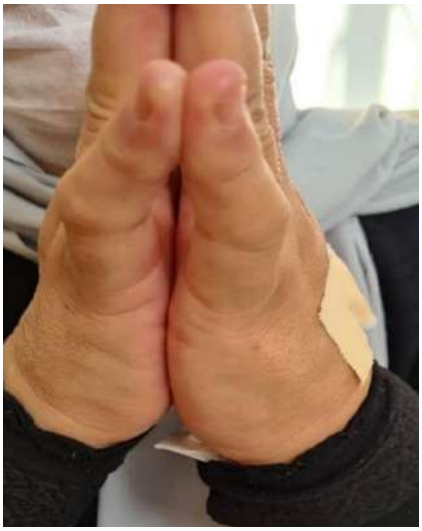

Figure 6: Prayer sign

Among 15 (8.3%) diabetic patients having nail changes; (16.3%) of males and (5.8%) of females. Ten (66.7%) patients have yellow nails, and 5 (33.3%) patients have thick nails (Figure 7).

Figure 7: Nail changes showing thick nail palate.

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Eight (4.4%) of diabetic patients had foot ulcers (7%) of males and (3.6%) of females. Diabetic bullae seen in 4 (2.2%) patients (2.3%) of males and (2.2%) of females. Among 4 (2.2%) diabetic patients having viral infections, all were females (2.9%). Two (1.1%) patients have planter warts, and 2 (1.1%) patients have herpes zoster. Two (1.1%) patients had bacterial infections all were males (4.7%). One (0.55%) patient had carbuncle (Figure 8), and 1 (0.55%) patient had ecthyma.

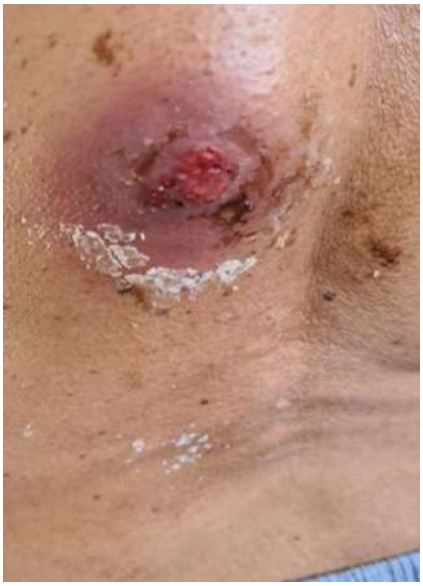

Figure 8: Carbuncle on the back.

DISCUSSION

In the current study, most of the diabetes patients age group was 41-60 years for females, while males were those over 60 years old, these observations were consistent with a regional study from El-Beida city (6). The majority of patients enrolled in the present study were females. Skin findings were seen more commonly in females in the current study, as the higher number of females presenting to the OPD indicates greater health awareness among females; this result appears to be similar to the study of Niaz, F, et al. (7). In this study, the most common five skin disorders observed associated with diabetes are: acanthosis nigricans (69.4%), skin tag (56.7%), xerosis (54.4%), pruritus (37.2%), and fungal infections (25.6%), this comes in accordance with studies in Libya (6), Saudi Arabia (8), and Turkey (9). In the present study, the most common dermatosis associated with DM was acanthosis nigricans, seen in (44.2%) of males and (77.4%) of females, followed by skin tags, which accounted for (37.2%) of males and (62.8%) of females. Thappa et al. (10) concluded that skin tags may serve as a marker for diabetes mellitus.

Xerosis was seen in 65.1% of males and 51.1% of females, consistent with a study from El-Beida City (6). The high prevalence of xerosis in our diabetic patients is most likely because most of the patients don't drink an adequate amount of water per day, especially in the winter season, or due to the normal xerotic process of the elderly. Pruritus was also seen in 58.1% of males and 30.7% of females. Pruritus is well known to have an association with diabetes mellitus as reported in the past literature (11, 12). Al-Mutairi et al. who reported pruritus in (47%) of their patients (13); this is nearly similar in frequency when compared to our patients (37.2%). In the present study, 25.6% of the enrolled patients had fungal skin infections; all were females (33.6%). The most common disease was tinea pedis, which was seen in (16.7%) of patients. Tinea pedis can act as a portal of entry for secondary bacterial invasion. Candidiasis, which may be an early indicator of undiagnosed diabetes, was also seen in 8.9% of our patients. Diabetic dermopathy was seen in 17.7% of our patients (18.6% of males and 17.5% of females); this is in contrast to the results obtained by Niaz, F, et al., where diabetic dermopathy frequency was 9% in their patients (7).

In this study, 10.6% of the enrolled patients had prayer sign (2.3% of males and 13.1% of females), which is inconsistent with Ezejiofo ROI, who reported that prayer sign was seen in only 4% of patients (14). Fifteen (8.3%) diabetic patients had nail changes (16.3%) of males and (5.8%) of females, lower than that reported by Niaz, F., et al., where nail changes were seen in (16%) of their patients (7).

In the current study, 8 (4.4%) diabetic patients had

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foot ulcers (7%) of males and (3.6%) of females. It is usually related to different mechanisms like impaired immunity, neuropathy, peripheral arterial disease, venous insufficiency, and lymphedema. It has been reported with a variable frequency in different studies ranging between 10 and 50% (11, 15, 16). Consistent with current study, Niaz, F, et al have reported foot abnormalities were more common in female diabetics (7), while study done by Mansour et al. have reported foot abnormalities were common in male diabetics (17). Diabetic bullae were found in 2.2% of our patients (2.3% of males and 2.2% of females); this is in agreement with the results obtained by Bhat et al. (18). Viral infections were seen in (2.2%) of the patients; all of them were females (2.9%), this is in agreement with other regional studies (6). In this study, 2 (1.1%) diabetic patients had bacterial infections (4.7%); all of them were males. One (0.55%) patient had a carbuncle, and one (0.55%) patient had ecthyma; these findings are in contrast to the frequency of bacterial infections that was reported to be higher by a study from El-Beida city (6).

CONCLUSION

The prevalence of certain dermatoses was high among diabetic patients. So, diabetic patients are considered to be at risk of developing certain skin diseases.

RECOMMENDATION

General practitioners should be aware of the diagnosis and management of skin diseases that are commonly seen among diabetic patients, and difficult cases should be referred to specialists for early management to minimize complications and morbidities associated with diabetes mellitus.

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The Prevalence of Amoebiasis in Children Admitted to Gastro Department at Children's Hospital of Benghazi.

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Zahoor H. Almabrouk [3].

Original Research Article

Abstract

Background: Amoebiasis, caused by the protozoan parasite Entamoeba histolytica, remains a major public health concern, particularly in less developed and developing regions where sanitation standards are inadequate.

Aim: To investigate the role of E. histolytica as a primary cause of gastroenteritis and to assess infection rates among children admitted to the Gastroenteritis Department at Benghazi Children's Hospital over a one-year period.

Method: A cross-sectional study was conducted by using records from the Parasitology Department between January and December 2023. A total of 1,443 stool samples were examined microscopically and categorized into four age groups: 1–3, 4–6, 7–9, and 10–14 years.

Results: The overall prevalence of E. histolytica/dispar was 35.3%. Giardia lamblia infections accounted for 2.8%, while other microbial infections—including fungal organisms such as Candida spp.—represented 1.2%. The highest infection rate was recorded in the Gastroenteritis Department (59.0%), compared to 30.1% in the Outpatient Department. Seasonal trends showed a peak prevalence of 5.5% in August and the lowest rate of 1.3% in April.

Conclusion: The study highlights the substantial burden of E. histolytica infections among children in Benghazi, emphasizing the urgent need for improved sanitation, enhanced public health strategies, and continuous monitoring to reduce infection rates.

Keywords: Parasites, Amebiasis, Entamoeba histolytica, Gastroenteritis.

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INTRODUCTION

Amoebiasis, caused by the protozoan parasite Entamoeba histolytica, constitutes a major human intestinal disease with significant public health implications, particularly in regions with inadequate sanitation. As a primary contributor to severe diarrheal illness, amoebiasis is responsible for an estimated 40,000–100,000 deaths annually worldwide [1]. The clinical presentation varies widely, encompassing asymptomatic carriage, mild gastrointestinal disturbances, and severe outcomes such as amoebic colitis and amoebic liver abscess (ALA), which can progress to invasive extra-intestinal disease [2]. The public health importance of amoebiasis is further magnified by its role in childhood diarrhea and its classification as a reportable disease in systems like Libya's National Notifiable Disease Reporting System (NNDRS) [3].

Transmission occurs primarily through the fecal-oral route via the ingestion of contaminated food or water containing resilient Entamoeba cysts (10–18 μm), which are resistant to standard chlorination [4]. Upon ingestion, these cysts undergo excystation in the small intestine, releasing motile trophozoites that colonize the large intestine and penetrate the intestinal mucosa, leading to the formation of characteristic flask-shaped ulcers [5]. Given its low infectious dose and environmental stability, E. histolytica is classified as a Category B priority biodefense pathogen by the NIAID [5]. Clinically, amoebic colitis typically presents with symptoms such as colicky abdominal pain, frequent bowel movements, and diarrhea often containing visible blood and mucus [1].

Globally, the prevalence of E. histolytica infection is highly disparate, with reported rates in Africa reaching 12.4% in South Africa and 58.3% in Kenya [6]. High regional prevalence is often attributed to risk factors such as inadequate sanitation and poor hygiene [6].

International studies have confirmed seasonal patterns in E. histolytica infections; for instance, 65.5% of documented cases in China occurred between May and October, peaking in June [7]. Additionally, a large-scale study in northern Jordan, examining 21,906 patients, found the highest prevalence of both G. lamblia and E. histolytica during the summer months [8].

Local epidemiological data from Libya highlight significant gaps in understanding the prevalence and impact of E. histolytica infections. A study conducted in Sebha and Mourzak reported an overall intestinal parasite infection rate of 16.0% in children, with E. histolytica/dispar (12.8%) being significantly more prevalent than Giardia lamblia (3.2%) (p=0.004) [9]. This study also noted a non-significant trend toward higher infection rates in males (18.6%) compared to females (12.9%) (p=0.401), while identifying a significant association between prevalence and seasonal variation (p=0.027), with peaks observed in March [9].

Supporting these findings, a separate survey in Zella City reported an overall parasitic prevalence of 87%, with E. histolytica dominating at 65%, particularly during the autumn and spring seasons [10]. These results underscore the persistent challenge of intestinal parasitic infections in Libya, despite improvements in cultural and social awareness.

Given these local and regional insights, the current study aims to address knowledge gaps regarding E. histolytica infections among children in Libya. Specifically, this study sought to determine the prevalence and seasonal trends of E. histolytica among children admitted to the Gastroenteritis Department at Benghazi Children's Hospital over one year. Furthermore, it aimed to investigate associations with age, gender, and the hospital department, thereby contributing valuable data to enhance understanding and management of amoebiasis in the local context.

METHOD

Study Setting

This cross- sectional study was carried out at Benghazi Children's Hospital in Benghazi, Libya, following formal approval from the hospital administration. Data was collected over a 12-month period, from January to December 2023. Cases of Entamoeba histolytica infection were identified through the examination of records obtained from

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the medical laboratories of the hospital's Parasitology Department.

Study Subjects

The study comprised stool samples primarily referred from the gastroenteritis department, while samples from other hospital departments were also included for comprehensiveness. Training in parasite detection, laboratory diagnosis, information collection, sample acquisition procedures, and necessary precautions was provided under the supervision of parasitology specialists. This included observation within the hospital's gastrointestinal tract department. Suspected cases of parasitic infection were categorized into four age groups for analysis: 1-3 years, 4-6 years, 7-9 years, and 10-14 years.

Stool Examination

Parasitological examination was conducted using direct wet mount microscopy on all referred samples, processed immediately after collection. A small fecal aliquot was mixed with iodine solution and examined under low (×10) and high (×40) power magnification to identify E. histolytica. Positive cases were defined by the presence of trophozoites or cysts, but microscopy cannot differentiate between E. histolytica and E. dispar. To enhance diagnostic accuracy, normal saline wet mounts were prepared, and concentration techniques were employed. Multiple slides were examined by trained technicians in a blinded manner to minimize bias, with inter-observer agreement assessed to ensure consistency. These considerations are crucial for accurately diagnosing E. histolytica infections and understanding the limitations of the microscopy techniques used.

Limitations of the Study

Several limitations were encountered in this study. Some cases were excluded due to missing or unrecorded patient age and gender data, along with ambiguous documentation of parasitic infections. Operational challenges arose during technician training, impacting consistency in sample processing. Additionally, logistical constraints in collaboration between the gastrointestinal department and the laboratory affected research activities. There was also insufficient information regarding patient residence, whether local to Benghazi or from external areas. It is important to note that the samples collected were from patients admitted to the hospital or attendees of the departments during their illness, which explains the difficulties in obtaining comprehensive information. These factors highlight the constraints imposed by the available data from Benghazi Children's Hospital.

Statistical Analysis

Collected data were coded, tabulated, and analyzed using the Statistical Package for the Social Sciences (SPSS 25) software. Descriptive statistics, employing counts and percentages, were used to summarize quantitative data. Analytical statistics involved the application of the Chi-square test to compare groups based on qualitative variables.

RESULTS

Analysis of 1,443 stool samples from children admitted to the gastroenteritis department revealed the following age distribution among participants (aged 1-14 years): the 1-3year age group comprised 395 cases (27.4%), the 4-6year group had 589 cases (40.8%), the 7-9year group included 441 cases (30.6%), and the 10-14year group accounted for 18 cases (1.2%) The results are presented in Table (1).

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Table 1. Distribution of participating according to age.

Age in years	Frequency	Percent	Valid Percent	Cumulative Percent
1-3	395	27.4	27.4	27.4
4-6	589	40.8	40.8	68.2
7-9	441	30.6	30.6	98.8
10-14	18	1.2	1.2	100.0
Total	1443	100.0	100.0	

Table 2 detail gender distribution, identifying 804 males (55.7%) and 639 females (44.3%). Table shows the age group between 4-6 years had the highest participation rate, where the percentage of boys was (22.5%) and girls (18.4%), followed by the age group between 7-9 years that was (18.2%) for boys and (12.3%) for girls While the lowest participation rate was in the age groups of 10-14 years and was (1.2%).

Table 2. Frequency and percentage of participating according to gender.

Gender	Frequency	Percent	Valid Percent	Cumulative Percent
Boy	804	55.7	55.7	55.7
Girl	639	44.3	42.9	100.0
Total	1443	100.0	100.0	

Table 3. Distribution of participating according to age and gender.

Age group Boy		Gender		Total
		Girl		
1-3	Count	210	185	395
	Total	14.6	12.8	27.4
4-6	Count	324	265	589
	Total	22.5	18.4	40.8
7-9	Count	263	178	441
	Total	18.2	12.3	30.6
10-14	Count	7	11	18
	Total	0.5%	0.8%	1.2
Total	Count	804	639	1443
	Total	55.7	44.3	100.0

No significant difference was identified between both groups ($p > 0.05$)

Pathogen distribution is shown in Table 4. Entamoeba histolytica/dispar was detected in 35.3% of samples, while Giardia spp. was found in 2.8%. Other microbial infections (including Candida spp.) accounted for 1.2%, with 60.7% of samples negative for the targeted parasites.

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Table 4. Distribution of participating according to type of parasites.

Type of parasite & other microbial.	Frequency	Percent	Valid Percent	Cumulative Percent
Candida spp.	17	1.2	1.2	1.2
E. histolytica/dispar	510	35.3	35.3	36.5
Giardia lamblia	40	2.8	2.8	39.3
Nil	876	60.7	60.7	100.0
Total	1443	100.0	100.0	

Table 5 illustrate the distribution across hospital departments. The gastroenteritis department contributed the majority of samples (59.0%), followed by the Outpatient Department (OPD) (30.1%), Medical Unit (MU) (6.2%), Intensive Care Unit (ICU) (3.0%), and Hematology (0.4%)

Table 5. Distribution of participating according to department.

Department	Frequency	Percent	Valid Percent	Cumulative Percent
Gastroenteritis	852	59.0	59.0	59.0
Hematology	6	.4	.4	59.5
ICU	44	3.0	3.0	62.5
MU	90	6.2	6.2	68.7
Nephron	16	1.1	1.1	69.9
OPD	435	30.1	30.1	100.0
Total	1443	100.0	100.0	

Seasonal variation in case presentation is displayed in Table 6. August recorded the highest caseload (14.3%), followed by October (10.9%). The lowest incidence was observed equally in March and April (5.5%).

Table 6. Distribution of participating according to months of years.

Months of the year	Frequency	Percent	Valid Percent	Cumulative Percent
January	125	8.7	8.7	44.8
February	98	6.8	6.8	36.1
March	80	5.5	5.5	62.5
April	80	5.5	5.5	5.5
May	123	8.5	8.5	71.0
June	94	6.5	6.5	57.0
July	82	5.7	5.7	50.5
August	207	14.3	14.3	19.9
September	126	8.7	8.7	100.0
October	157	10.9	10.9	91.3
November	135	9.4	9.4	80.4
December	136	9.4	9.4	29.3
Total	1443	100.0	100.0	

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The relationship between age and parasite infection is presented in Table 7. The 4–6-year age group exhibited the highest E. histolytica/dispar infection rate (15.0%), followed by the 7–9-year group (10.6%). The 10-14year group had the lowest rate (0.6%). The overall Giardia infection rate remained 2.8%.

Table 7. Distribution of participating according to relationship between age groups and types of parasites.

Age group and Type Cross-tabulation						
Age group Candida spp.		Type				Total
		E. histolytica/dispar	Giardia spp.	Nil		
1-3	Count	5	131	12	247	395
	Total	0.3	9.1	0.8	17.1	27.4
4-6	Count	2	217	15	355	589
	Total	0.1	15.0	1.0	24.6	40.8
7-9	Count	10	153	13	265	441
	Total	0.7	10.6	0.9	18.4	30.6
10-14	Count	0	9	0	9	18
	Total	0.0	0.6	0.0	0.6	1.2
Total	Count	17	510	40	876	1443
	Total	1.2	35.3	2.8	60.7	100.0

No significant difference was identified between both groups. P=.236 (p> 0.05)

Table 8 describe the association between gender and department. Males had higher admission rates to the gastroenteritis department (33.0% vs. 26.1% for females). Similarly, OPD presentation was higher in males (17.3%) compared to females (12.9%), potentially reflecting behavioral differences.

Table 8. Participating according to relationship between gender and department.

Department and Gender Cross-tabulation					
			Gender		Total
			boy	Girl	
Department	Gastro	Count	476	376	852
		Total	33.0	26.1	59.0
	Hematology	Count	4	2	6
		Total	0.3	0.1	0.4
	ICU	Count	21	23	44
		Total	1.5	1.6	3.0
	MU	Count	47	43	90
		Total	3.3	3.0	6.2
	Nephron	Count	7	9	16
		Total	0.5	0.6	1.1
	OPD	Count	249	186	435
		Total	17.3	12.9	30.1
Total		Count	804	639	1443
		55.7	44.3	100.0	

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No significant difference was identified between both groups. P=.666 (p> 0.05)

Table 9 represent the relationship between age groups and department. Children aged (4-6) years recorded the highest percentage of admission to the gastrointestinal ward with a percentage (24.5%). While the percentage was close in the same ward in the age groups (7-9, 1-3) the percentage was (17.7%, 16.2. respectively). As for the OPD, the age group (4-6) had the highest percentage was (12.0%). While the nephron department has the lowest admission rate among the age groups (1.1%). There is statistically significant difference was identified between groups (P≤ 0.05).

Table (9). Distribution of participating according to relationship between age group and department.

Department 1-3		Age group				Total
		4-6	7-9	10-14		
Gastro	Count	234	353	255	10	852
	Total	16.2	24.5	17.7	0.7	59
Hematology	Count	0	2	3	1	6
	Total	0.0	0.1	0.2	0.1%	0.4
ICU	Count	23	11	8	2	44
	Total	1.6	0.8	0.6	0.1	3.0
MU	Count	20	47	23	0	90
	Total	1.4	3.3	1.6	0.0	6.2
Nephron	Count	4	3	9	0	16
	Total	0.3	0.2	0.6	0.0	1.1
OPD	Count	114	173	143	5	435
	Total	7.9	12.0	9.9	0.3	30.1
Total	Count	395	589	441	18	1443
	Total	27.4	40.8	30.6	1.2	100

Finally, Table10 demonstrate the seasonality of E. histolytica/dispar infections. The peak infection rate occurred in August (5.5%), followed by September (4.2%), with the lowest rate in April (1.3%). The cumulative prevalence of E. histolytica/dispar infection over the study period was 35.3%.

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Table (10). Distribution of participating according to relationship between months and E. histolytica/ dispar.

Months	E. histolytica/dispar Frequency (%)
January	35 (2.4)
February	30 (2.1)
March	29 (2.0)
April	19 (1.3)
May	45 (3.1)
June	31 (2.1)
July	44 (3.0)
August	79 (5.5)
September	60 (4.2)
October	54 (3.7)
November	45 (3.1)
December	39 (2.7)
Total	510 (35.3)

There is statistically significant difference was identified between months ($P \leq 0.05$).

describe the association between gender and department. Males had higher admission rates to the gastroenteritis department (33.0% vs. 26.1% for females). Similarly, OPD presentation was higher in males (17.3%) compared to females (12.9%), potentially reflecting behavioral differences.

DISCUSSION

The findings of this study provide critical insights into the demographic, seasonal, and clinical patterns of parasitic infections, particularly E. histolytica/dispar and Giardia lamblia, among children admitted to Benghazi Children's Hospital. The results underscore significant associations between age, gender, seasonal factors, and healthcare utilization, which align with broader epidemiological trends while highlighting region-specific risk factors.

Compared to recent international studies, the prevalence of Entamoeba histolytica/dispar in our cohort of children at Benghazi Children's Hospital (35.3%) is substantially greater than the 13.0% infection rate documented by Uchejeso et al in Nigeria, where differences are attributed to sanitation standards and sample characteristics [11]. In Kabul, Afghanistan, Mamozai et al described a lower infection prevalence in young children, emphasizing disparities linked to urban health resources and public health infrastructure [12]. Methodologically, our work utilized retrospective microscopy of stool samples throughout one year, whereas other studies applied more advanced molecular diagnostics, such as PCR and ELISA, offering greater sensitivity and species differentiation [13]. Seasonal variation found in our dataset aligns with Ethiopian findings, where peaks in amoebiasis prevalence have been connected to climate influences on transmission [14]. Overall, these international comparisons reinforce the significance of local sanitation conditions, diagnostic approaches, and healthcare systems in shaping regional prevalence rates and highlight the need for targeted public health interventions.

Demographic and Gender Disparities

The age distribution of cases revealed a pronounced vulnerability among children aged 4–6 years, who constituted the largest proportion of infections (40.8%) and exhibited the highest prevalence of E. histolytica/dispar (15.0%). This aligns with global evidence indicating heightened exposure to fecal-oral pathogens in early childhood due to exploratory behaviors, inadequate hygiene practices, and increased environmental interaction. Notably, the sharp decline in cases among older children (10–14 years: 1.2%) may reflect improved immunity or reduced exposure as children age. Gender disparities were evident, with boys (55.7%) disproportionately affected, particularly in high-risk departments like gastroenterology (33.0% boys vs. 26.1% girls). This aligns with the hypothesis that boys' outdoor activities in unsanitary environments elevate their exposure to contaminated water or soil, a phenomenon documented in low-resource settings with limited public health infrastructure.

Infection Patterns and Seasonal Trends

The dominance of E. histolytica/dispar (35.3%) over Giardia lamblia (2.8%) underscores the endemicity of amebiasis in the region, likely exacerbated by socioeconomic factors such as contaminated water sources, overcrowded housing, and poor hygiene practices. The high proportion of negative

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results (60.7%) suggests potential underdiagnosis, non-parasitic etiologies, or the influence of unmeasured variables like viral or bacterial pathogens. Seasonal variation in infections, peaking in August (14.3%) and October (10.9%), correlates with warmer temperatures and potential fluctuations in water quality or increased outdoor activity during summer months. The low April prevalence (1.3%) may reflect cooler weather reducing pathogen survival or seasonal hygiene campaigns, though further investigation is warranted.

Clinical and Public Health Implications

The predominance of gastroenteritis admissions (59.0%) highlights the burden of diarrheal diseases in this population, consistent with global data linking poverty and inadequate sanitation to gastrointestinal infections. The statistically significant age-department association ($p \leq 0.05$), particularly the high gastroenterology admissions among 4–6-year-olds (24.5%), reinforces the need for targeted interventions in this age group. Conversely, the minimal hematology involvement (0.4%) suggests parasitic infections in this cohort primarily manifest as acute gastrointestinal illness rather than systemic complications.

Limitations and Future Directions

While this study offers valuable insights, its hospital-based design limits generalizability to community settings, where asymptomatic or mild cases may go undetected. The reliance on hospital records may introduce selection bias, and the lack of granular socioeconomic data (e.g., household income, water source details) restricts the ability to fully elucidate risk factors. Future research should incorporate community-based longitudinal studies to capture broader epidemiological trends and evaluate interventions such as water purification programs, hygiene education, and routine deworming. Additionally, molecular diagnostics could clarify the prevalence of E. histolytica versus non-pathogenic Entamoeba dispar and Giardia lamblia, refining clinical management. Potential contributing factors to the high prevalence (e.g., socioeconomic conditions, water source quality, hygiene practices) were noted.

CONCLUSIONS

This study underscores the interplay of demographic, environmental, and seasonal factors in shaping the burden of parasitic infections among children in Benghazi. Addressing these challenges requires multisectoral efforts to improve sanitation infrastructure, promote hygiene education, and strengthen healthcare capacity for early diagnosis and treatment. Prioritizing high-risk groups—particularly young children and boys—could mitigate morbidity and reduce the strain on pediatric healthcare services.

From the present study, it could be concluded that amoebiasis remains one of the most significant enteropathogenesis worldwide. Most of the cases that were admitted to the gastroenteritis department, at the Benghazi Children's Hospital accounted for (35.3%) of the disease rate in this department.

RECOMMENDATIONS

The relatively uncomplicated lifecycle of Entamoeba species facilitates efficient transmission between human hosts, thereby ensuring their continued persistence as commensal-like organisms. Despite ongoing research, no effective vaccine is currently available, and treatment options remain limited to a single major class of drugs. These constraints make prevention particularly difficult and emphasize the urgent need for greater public health awareness, as well as the development of innovative therapeutic and preventive measures to control amoebic infections. Amoebiasis constitutes a health problem among children in Benghazi city. Therefore, the study recommended the following:

It has become clear to us from the current study and previous studies in Libya that the Entamoeba parasite is widespread, so we recommend combating the parasite in cooperation with the Ministry of Health.

Efforts should be made to raise clinicians' awareness of this parasitic diseases.

Technicians must be trained on how to detect parasites in multiple ways and not limited to the routine method.

Personal hygiene should to be promoted in the region through campaigns by the government.

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There is a need for continuous stool examination of children suffering from diarrhea in hospital and treatment given as infection rate was high to control the disease.

Illegal immigrants and expatriate workers may be one of the reasons for the spread of the disease, and we recommend conducting routine examinations to avoid the transmission of any diseases.

Avoid eating street foods especially in public places.

Parasitology is neglected in many laboratories, so we recommend that it be in the first ranks and that cooperation with the Ministry of Health be done in this so that parasitic diseases do not spread.

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The Role of Multi Detector Computerized Tomography in Evaluation of Maxillofacial Fractures.

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Original Research Article

Abstract

Objective: The current study's goals are to assess the effectiveness of Multi Detector Computerized Tomography (MDCT) in treating patients who have experienced maxillofacial trauma, describe demographic variations, describe the frequency and types of fractures that were subjected to CT scans in the Benghazi region of Libya, and compare the results with those of comparable studies carried out elsewhere in the world.

Materials and Methods: We collected information from the radiology department of the al-Jala teaching hospital in Benghazi to conduct a descriptive, cross-sectional hospital-based study Between 2010 and 2013, 417 patients' medical records who underwent head and face CT scans after suffering maxillofacial trauma were examined for the study (4 years).

Results: The peak frequency, which occurred in the age group of 21 to 30, covered a range of ages from 2 to 85 years. The median age, measured by mean and standard deviation, was 29.9 +/- 12.2 years. There were six men for every woman. Road traffic accidents (RTAs) were the leading cause of fractures (75%), followed by assault (7.67%), and we found no association between gender and the cause of fracture ($p = 0.537$). While the orbital walls (61%) were the most frequently broken bone in simple maxillofacial fractures, the zygomaticomaxillary complex (ZMC), which makes up 22.2% of the midface, was the most vulnerable area in complex facial fractures. There was no connection between gender and the location of the fracture.

Conclusion: Maxillofacial trauma can occasionally occur with serious cosmetic and functional repercussions. MDCT is required for the identification and classification of maxillofacial fractures and provides an accurate diagnosis for the design of treatment plans. Early surgical intervention is crucial for the successful management of these fractures.

Keywords: Fracture, Midface, Benghazi, Image.

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INTRODUCTION

Facial fractures can be detected using The Multi Detector Computerized Tomography (MDCT) as it's considered to be the golden standard method due to its non-invasive technique, accessibility, speed of acquisition, and exceptional accuracy in detecting even minute fractures. Additionally, acute intracranial pathology, which might be more urgent, is assessed concurrently. [1,2] Blunt or penetrating trauma that uses moderate-to-strong force is the most common cause of facial fractures. These fractures may result from a gunshot wound, a fall, a physical assault, or a motorcycle accident. The MDCT can promptly spot any related facial buttresses and soft tissue injuries that might require surgery. When a complicated fracture develops, many issues could arise, such as lefort fractures, are kind of midfacial fractures which damage the pterygoid plates in their entirety and can separate the maxilla from the skull in whole or in part like in Lefort III type , increasing the risk of intracranial infections, or like type II involving the medial part of midface, and Lefort I in which the palate is separated from the dentition Hemorrhage and cerebrospinal fluid leakage rise when a frontal sinus fracture extends through the posterior sinus wall. Other types of complex fractures include the zygomaticomaxillary complex, which disrupts all four zygomatic sutures and may result in enophthalmos due to increased orbital volume because of the angulation of the lateral orbital wall, and the naso-orbito-ethmoid complex fractures, which frequently involve the medial orbital wall, the nasal bone, the ethmoid sinuses, and the location where the medial canthal tendon attaches. [1,3] While it is the radiologist's obligation to recognize and accurately diagnose facial fractures on imaging, it is equally important to simply and clearly state the findings in the radiology report. An excellent report should show understanding of the clinically significant factors that might influence management. The craniofacial anatomy includes a complex section known as the midface. It consists of numerous distinct bone components that interact with one another, communication. The midface merits special consideration when it comes to evaluation and management because, in addition to its structural characteristics, it serves functional purposes related to breathing, speech, swallowing, mastication, olfaction, and vision.

Therefore, any injury or deformity in this area can have a significant impact on a person's quality of life. Due to the complexity of the midface anatomy, specialized imaging techniques like CT scans are often required to accurately diagnose. The posterior boundary is made up of the frontal bone superiorly and the sphenoid inferiorly, while the lateral boundary is the temporal bone. Midface structure has thin bone parts supported by a hard frame of buttresses. structural pillars of the mid-face are canines, zygomatic, and pterygoid buttresses [4]

The midface is made up of several bony structures including two maxillae, zygomatic bones, zygomatic processes of temporal bones, lacrimal, palatine, and nasal bones, the vomer bone, the ethmoid, with the connected conchae, two inferior conchae, and the pterygoid plates of the sphenoid bone [5].

MATERIAL AND METHOD

Data were collected from the Radiology Department at Al-Jala Teaching Hospital in Benghazi to conduct a descriptive, cross-sectional, hospital-based study. Between 2010 and 2013, the medical records of 417 patients who underwent head and facial CT scans following maxillofacial trauma were reviewed. The study utilized a General Electric (GE) 128-slice helical CT scanner. CT scans of the face were performed with the patient in a supine position, and axial slices were acquired at 0.625 mm collimation, with a field of view extending from the top of the frontal sinuses to the chin. Supine axial imaging was selected to ensure rapid acquisition and patient comfort, with a total exposure time of approximately 16 seconds. Coronal and sagittal reconstructions were generated, and 3D volume-rendered images were also obtained.

Imaging modality:

Computed tomography (CT) scans, which offered fine-grained visualisation of fracture patterns, were used to evaluate all fractures. Two primary catego-

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ries were used to classify fractures: Simple fractures: affecting the mandible, orbital walls, nasal bone, isolated zygomatic arch, frontal sinus, and maxillary sinus. Complex fractures include naso-orbito-ethmoidal (NOE) fractures, LeFort I, II, and III fractures, and zygomaticomaxillary complex (ZMC) fractures. Descriptive statistics were used to summarise clinical and demographic features in the statistical analysis, which was carried out using SPSS version 23 for Windows. Associations between variables were examined using chi-square tests or other suitable statistical techniques; a p-value of less than 0.05 was deemed statistically significant.

The study received approval from the Head of the Radiology Department as well as ethical approval from the hospital's Research and Ethics Committee.

RESULTS

Age and gender distribution:

The age of the patients was ranged from 2 to 85 years at the time of the injury, with a mean age (SD) of 29.9 years. The age group from 21 to 30 years had ranked the highest incidence of maxillofacial trauma (n = 180; 43.2%). Up until the third decade, the age-specific distribution of patients showed an upward trend, after which the incidence fell with each succeeding decade. Injuries happened 21 times (5%) in the first decade, 51 times (12.2%) in the second, 180 times (43.2%) in the third, 104 times (24.9%) in the fourth, 35 times (8.4%) in the fifth, 18 times (4.3%) in the sixth, 05 times (1.2%) in the seventh, and three times (0.7%) in the eighth. Pediatric (less than 18 years of age) fracture accounted for 12.7% (n = 53) of patients, and 2.87% (n=12) was more than 60 years of age table 1. Men were mostly affected than women in all age groups table1.

Table 1: Distribution of the Study Sample by their age group and sex.

Age group	Male	Female	Total	Percent%	Mean ± SD	P value
(1-10)	17	4	21	5%	29 ± 12.2	P=0.008
(11-20)	40	11	51	12.2%		
(21-30)	165	15	180	43.2%		
(31-40)	91	13	104	24.9%		
(41-50)	27	8	35	8.4%		
(51-60)	12	6	18	4.3%		
(61-70)	4	1	5	1.2%		
>70	3	0	3	0.7%		
Total	359	58	417	100		

The male to female ratio was 6:1. Figure 1 shows the distribution of the patients according to their sex.

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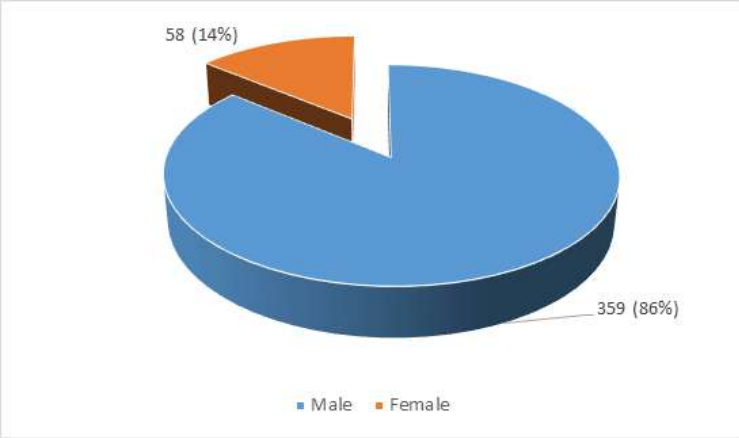

Figure 1: Distribution of the patients according to their sex.

ETIOLOGY

The most common reason for maxillofacial trauma were maxillofacial trauma (n = 314; 75.29%), followed by physical assault (n = 32; 7.67%), gunshot wound (n = 29; 6.95%), and unintentional falls (n = 29; 6.95%). Sports-related injuries occurred in 13 cases (3.1%) of the remaining fractures, which were caused by a variety of factors. Injury etiologies are displayed in Table 2 and Figure 2.

Regarding the etiologies of trauma, our findings showed a statistically significant difference between genders (p = 0.032).

Table 2: Distribution of the patients by their gender and cause of maxillofacial trauma

Etiology of Trauma	Road Traffic Accident	Fall from Height	Physical Assault	Sport Injuries	Bump Explosive	Gun Shot	Total	P value
Male	261 (62.5%)	25 (5.9%)	32 (7.67%)	2 (0.47)	11 (2.63%)	28 (6.71%)	359 (86%)	0.032
Female	53 (12.7%)	4 (0.95%)	0 (0)	0 (0)	0 (0)	0 (0.23%)	58 (14%)	
Total	314 (75.29%)	29 (6.95%)	32 (7.67%)	2 (0.47%)	11 (2.63%)	29 (6.95%)	417 (100)	

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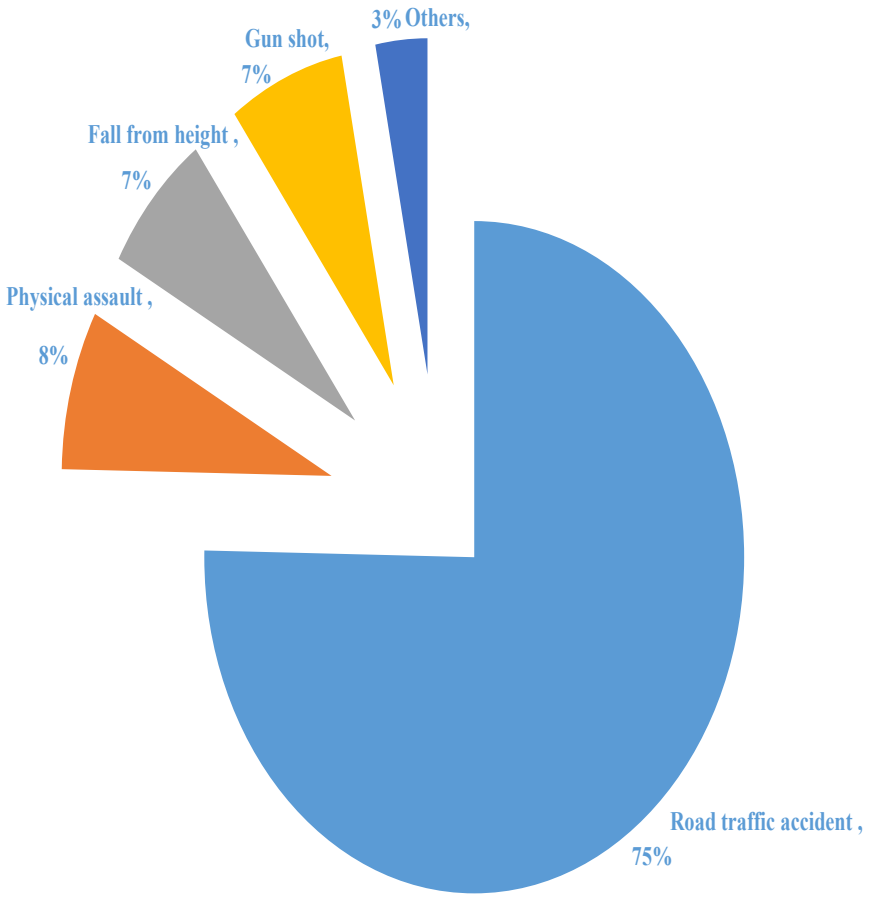

Figure 2: Etiologies of Maxillofacial Trauma.

Fracture site:

Among the simple maxillofacial fractures, the orbital walls were the bone that fractured most frequently. There were 254 cases overall (or 60.9%) where the orbital wall fracture was present. The second most affected area of maxillofacial trauma was the maxillary sinus wall (n = 216; 51.8%), followed by the nasal bone (n = 180; 43.2%), the isolated zygomatic arch (n = 132; 32%), the mandible fracture (n = 105; 25.2%), and the frontal sinus fracture (n = 80; 19.2%) , Table 3 and figure 3.

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Table3: Distribution of patients by their gender and the site of the simple Maxillofacial Fracture.

Computed Tomography Finding (CT)	Male	Female	Number (no)	Percent%
Orbital Wall Fracture	229	25	254	61.0%
Maxillary Sinus Fracture	195	21	216	52.0%
Nasal Bone Fracture	152	28	180	43.2%
Isolated Zygomatic Arch Fracture	117	15	132	32.0%
Mandible Fracture	90	15	105	25.2%
Frontal Sinus Fracture	72	8	80	19.2%

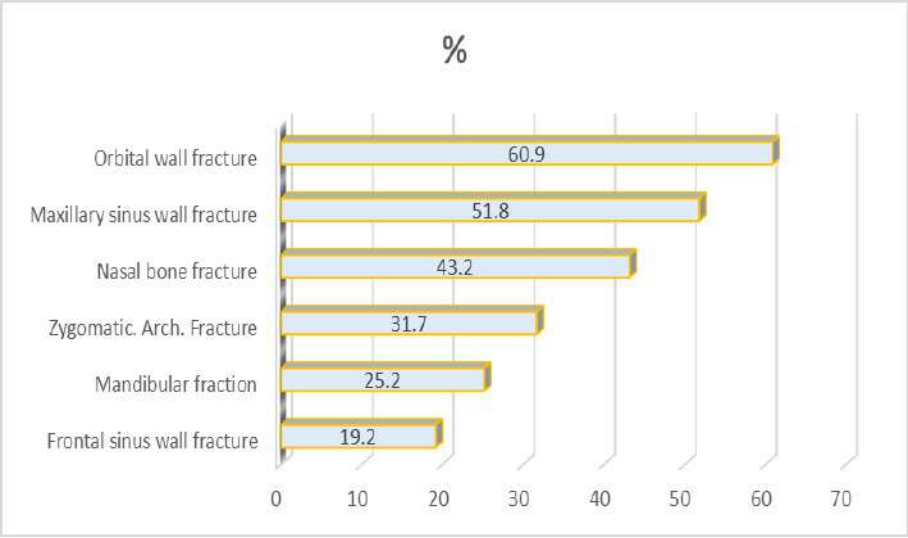

Figure 3: Distribution of the patients by the site of Simple Maxillofacial Fractures According to the MDCT Findings.

The most common complex maxillofacial fractures overall (n= 94; 22.5%) were zygomatic maxillary complex fractures, followed by naso-orbito-ethmoid complex fractures (n=31; 7.4%), maxillary fracture le fort III with total number of 26 and percentage 6.2% and le fort II (n=23; 5.5%), and le fort I (n=9; 2.2%), table 4 and figure 4.

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Table 4. Distribution of patients by their gender and the site of the complex Maxillofacial Fracture.

Computed Tomography Finding (CT)	Male	Female	Number (n)	Precent %
Zygomatic-Maxillary Complex Fracture	48	46	94	22.5%
Naso-Orbital-Ethmoidal Complex Fractur	28	3	31	7.4%
Le Fort Type III Fracture	23	3	26	6.5%
Le Fort type II Fracture	21	2	23	5.5%
Le Fort type I Fracture	8	1	9	2.2%

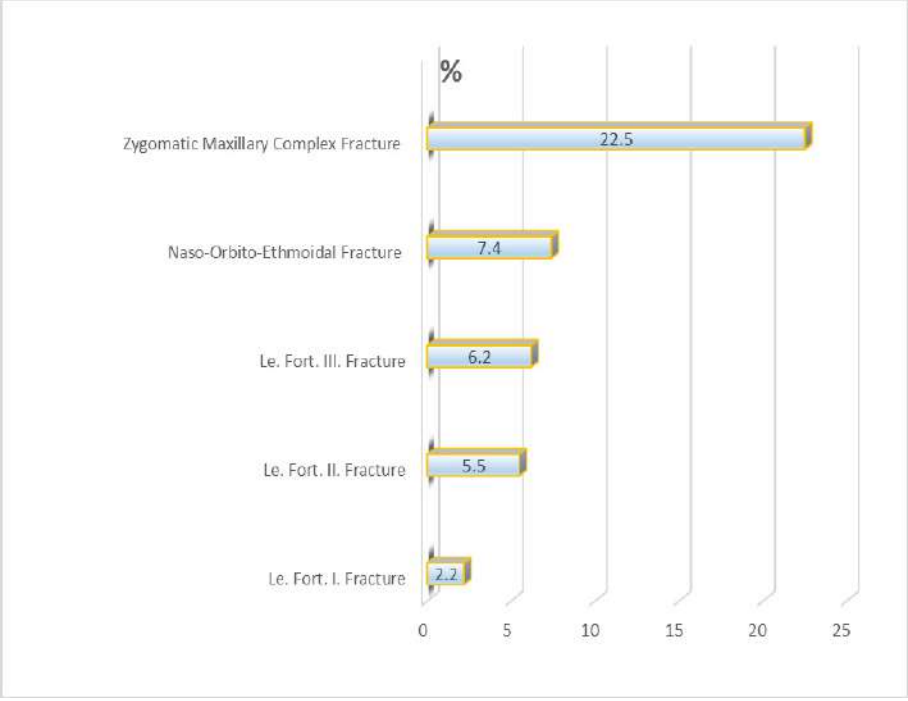

Figure 5: Distribution of patients according to the site of the complex Maxillofacial Fracture.

Regarding the distribution of fractures by age group, ZMC, lefort I, and II fractures were observed in all age groups with the exception of children aged 0 to 10 years. Patients between the ages of 21 and 30 made up the majority of mid facial fracture cases (43.2%), with orbital wall fractures making up the most common simple fracture pattern in this group and Zygomaticomaxillary complex the most common complex fracture pattern. It is also noteworthy that isolated orbital fractures were most common in the youngest age group (0 to 10), and maxillary sinus wall fractures were most prevalent in the oldest group (60+), table 5.

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Table 5. Distribution of the patients according to the site of the fractures and age Group Category.

Age Group	Orbital Wall Fracture	Maxillary sinus wall Fracture	Nasal Bone Fracture	Isolated zygomatic arch fracture	Mandible fracture	Frontal sinus	ZMC	NOE	Le Fort I	Le Fort II	Le Fort III
(1-10)	14	3	3	2	5	3	0	2	0	0	2
(11-20)	28	21	25	16	8	10	12	4	1	1	3
(21-30)	111	87	80	55	45	38	42	13	3	9	8
(31-40)	61	68	51	34	34	22	23	8	1	7	9
(41-50)	22	18	12	11	6	6	8	2	2	1	2
(51-60)	13	12	4	11	6	1	8	0	1	3	2
(61-70)	3	4	3	2	0	0	0	0	1	1	0
>70	2	3	2	1	1	0	1	2	0	1	0
Total	254	216	180	213	105	80	94	31	9	23	26

The ZMC fracture was the most prevalent complex bone fracture in both sexes; however, in men, the most common fracture pattern was an isolated orbital wall fracture. A solitary fracture of the nasal bone was the most frequent simple bone fracture in females, Fisher's exact test was utilized to investigate the relationship between gender and fracture site, Fisher's exact test ($p = 0.812$) found no association between gender and fracture site.

DISCUSSION

The most frequent cause of maxillofacial fractures, according to this study, was traffic accidents, the occurrence of maxillofacial trauma in developing nations is influenced by a lack of traffic laws, along with inadequate road infrastructure, older cars lacking safety standards, and cell phone use while driving [6]

Previous research has revealed that in affluent countries, violence is more common than traffic accidents as a reason for maxillofacial fractures [7]

In this study, the ratio of male to female patients in maxillofacial fractures was 6:1.

An additional study also came to a similar conclusion which done by [8,9] Men typically became the family's breadwinner and tend to spend more time outside, which increases their risk of trauma, whereas women are more frequently at home and have fewer trauma risk factors.

a MDCT scanner and a modern workstation are now essential diagnostic tools for any emergency room, to provide the best acute therapy of the midfacial trauma, the surgeon must fully understand the morphology and severity of the fractures [10].

there are considerable geographical disparities in the frequency of midfacial fractures, the majority of research reported in the literature indicates that mandibular fractures occur more frequently than mid-facial fractures [11,12, 13].

In this study, 61% of all facial bone fractures involved the orbital bone coinciding with other studies [14,15,16] the second most typical type of fractured bone was the maxillary sinus wall, which made up 52% of all fractured bones; the third most often fractured isolated bone was the nasal bone, with an average incidence of 43.2%. Separate fractures of the zygomatic arch made up about 32% of the fractures, mandibular fractures made up 25.2%, and frontal sinus fractures made up 19.2%.

Zygomatico-maxillary complex fractures are the most prevalent type of complicated facial fractures, accounting for 22.5% of occurrences, similar to sizable studies [17,18,19]. followed by the naso-orbital-ethmoidal complex fracture at 7.4%. Le Forte III contributed 6.5%, Le Forte II 5.5%, and Le Forte I 2.2% to the total.

We proved that the CT scan is an effective diagnostic tool for assessing face fractures. Because it makes 3-D investigation and high-resolution multiplanar reconstructions possible.

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CONCLUSION

In Benghazi, one of the major health problems is maxillofacial trauma. Maxillofacial fractures can become an aesthetic and functional issue if they are not promptly and effectively treated. Trauma affects a person's psychological well-being and has a detrimental socioeconomic effect on society, in people between the ages of 21 and 30 have the highest maxillofacial fractures (43.2%), according to our study. In the current study, 75% of the causes were related to road accidents. The zygomaticomaxillary complex (22.5%) was the most broken area of the midface, according to our study, which also found that ocular wall fractures predominated among people with simple maxillofacial trauma (61%). The findings of our investigation showed that car accidents were the main cause of maxillofacial injuries in Benghazi.

RECOMMENDATION

Public awareness campaigns are needed to educate the population—particularly drivers—about the importance of adhering to driving regulations and using safety equipment. These findings also highlight the need for authorities to strictly enforce existing traffic laws to reduce reckless, high-speed driving on highways.

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Thyroid disorders in patients with polycystic ovarian syndrome in Benghazi.

Omar Alfalah [1*], Fathia Ehmouda [2].

Original Research Article

Abstract

Background: Recent studies have highlighted a higher occurrence of thyroid abnormalities in women diagnosed with polycystic ovary syndrome (PCOS), although the underlying mechanisms linking the two conditions remain uncertain.

Aim and Objectives: To determine the prevalence of thyroid dysfunction among patients with PCOS.

Methods: A retrospective review of medical records was conducted for 116 patients attending the endocrine clinic in Benghazi medical center during the period from the first of September to the end of October 2020.

Results: The mean age was (35.5±9.8 years), the mean body mass index for the study group was 31.8±6.5kg/m2. Among studied group; 81% of participants had oligomenorrhea, 97.4% had hirsutism, and 84% had ultrasound features of polycystic ovaries; Overall, the prevalence of thyroid disorders among patients with PCOS was 31%, the main thyroid disorder was autoimmune thyroiditis which represented 13.8% followed by subclinical hypothyroidism which found in 9.5% of all participants.

Conclusion: More than one third of the studied group had thyroid disorders. Autoimmune thyroiditis represented the main disorder.

Keywords: PCOS, thyroid, thyroiditis, hypothyroidism, hyperthyroidism, goiter, autoimmune, subclinical.

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INTRODUCTION

Polycystic ovary syndrome (PCOS) is recognized as one of the most prevalent endocrine conditions in women, typically defined by irregular ovulation, androgen excess, and the presence of polycystic ovaries. It affects 15–20% of women of reproductive age (1). Evidence suggests an association between PCOS and thyroid disorders, particularly autoimmune thyroiditis and nodular goiter (2). Rates of subclinical hypothyroidism (SCH) and autoimmune thyroiditis have been reported to be more common in women with PCOS compared to the general population (3). The Rotterdam Consensus (2003) established the diagnostic framework for PCOS, requiring the presence of at least two of the following: (1) menstrual irregularities such as amenorrhea (absence of menstruation for ≥6 months), oligomenorrhea (cycle length >35 days), or prolonged cycles; clinical or biochemical signs of hyperandrogenism; and ultrasound findings of polycystic ovaries, defined as ≥12 follicles measuring 2–9 mm in diameter and/or an ovarian volume >10 mL (4). Subclinical hypothyroidism affects approximately 4–8% of women of reproductive age (5). Although often asymptomatic, it may present with subtle manifestations including dyslipidemia, hyperglycemia, insulin resistance, menstrual dysfunction, obesity, and infertility—symptoms that may overlap with PCOS (2,6). In primary hypothyroidism, elevated thyroid-stimulating hormone (TSH) and prolactin levels can influence ovarian physiology. Prolactin interferes with ovulation by altering the follicle-stimulating hormone (FSH) to luteinizing hormone (LH) ratio and increasing adrenal androgen secretion. Additionally, TSH may interact with FSH receptors, while prolonged hypothyroidism can lead to collagen accumulation in the ovaries, further aggravating cystic morphology. The degree of ovarian changes often depends on both the duration and severity of the thyroid dysfunction. Recent research has highlighted elevated markers of autoimmunity in women with PCOS, reinforcing the possible link between PCOS and autoimmune thyroid disease (2). In fact, one study showed that the prevalence of PCOS was significantly higher in adolescents (13–18 years) with hypothyroidism and positive thyroid peroxidase antibodies (anti-TPO Ab), compared with controls (46.8% vs. 4.3%) (7). The study aimed to estimate the frequency of thyroid disorders among patients with PCOS at Benghazi medical center.

PATIENTS AND METHODS

This study was conducted at the Benghazi Medical Center at the endocrine clinic during the period from the first of September to the end of October 2020, a retrospective study of patients' files. The total number of files was 1083, among them 116 patients were diagnosed with polycystic ovarian syndrome.

The questionnaire was adapted from an article (Thyroid profile in polycystic ovarian syndrome) (8).

The questionnaire was divided into three main sections: section A involving personal data (age, marital status, body mass index), section B involving features of polycystic ovarian syndrome (amenorrhea, oligomenorrhea or prolonged cycles, evidence of hyperandrogenism, ultrasonography features of PCOS), and section C involving the type of thyroid dysfunction.

Data analyzed using SPSS version 20. Variables were summarized as frequencies, percentages, means, and standard deviations.

RESULTS

I. General characteristics of PCOS patients

The mean age for the study group was 35.5 years with a standard deviation of 9.8 years (35.5±9.8 years), 45.7% were in the age group between 26 to 35 years and most of them were single (66.4%).

The mean BMI for the study group was 31.8±6.5kg/m2.

The result showed most of the patients with polycystic ovarian syndrome were classified as obese class I and overweight, with percentages (29.3%,26.7% respectively) as shown in Table 1.

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Table 1: Body mass index distribution.

Classification	No.	%
Normal	17	14.7
Over Weight	31	26.7
Obesity I	34	29.3
Obesity II	22	19.0
Obesity III	12	10.3
Total	116	100%

II. polycystic ovarian syndrome

1. Hyperandrogenism signs

The clinical signs of hyperandrogenism found in the patients who underwent the study were hirsutism, acanthosis nigricans, and acne. Hirsutism was almost found in all patients, with a percentage of 97.4%. And in some patients, there was more than one sign. While acanthosis nigricans and acne were less frequent with percentages of (18.1%, 7.8% respectively) as shown in Table 2.

Table 2: Hyperandrogenism signs distribution.

Sign	Yes	No	%
Hirsutism	113	3	97.4
Acanthosis nigricans	21	95	18.1
Acne	9	107	7.8

2. Menstrual cycle

Most patients (81%) presented with oligomenorrhea. Amenorrhea and menorrhagia represented 9.5% for each.

3. Pelvis ultrasound

Most patients had ovarian cysts by pelvic ultrasound, with a percentage of 84%.

III. Thyroid disorders among the studied group

Overall, the prevalence of thyroid disease in polycystic ovarian syndrome was 31% of all participants.

The highest percentage of the studied group (69%) had normal thyroid function, while autoimmune thyroiditis and subclinical hypothyroidism represented (13.8%, 9.5% respectively) Hypothyroid patients represented 1.7% due to either post-surgical hypothyroidism or post-radioactive iodine hypothyroidism. Figure 1

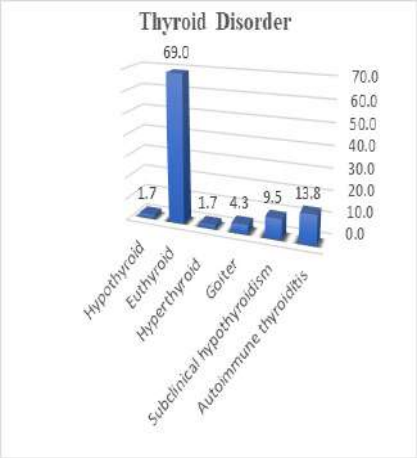

Figure 1: Distribution according to thyroid disorders.

DISCUSSION

The present study found that polycystic ovary syndrome (PCOS) was most frequently observed in women aged 26–35 years, while its prevalence decreased notably during puberty. It was predominantly a condition of reproductive age, with high rates among women of marriageable age in arabic muslim communities. Consequently, many women presented to outpatient clinics with infertility or menstrual abnormalities.

A significant relationship was observed between obesity and thyroid dysfunction. In the present study obesity affected more than a half which was near to that reported by Najem et al. (9) where obesity reported in 57% of their study participants. Thyroid function appeared to influence BMI like diabetes and physical activity (10). While the prevalence of overweight in adolescents with PCOS was 33.3% in Rahmanpour et al which was near to the present study (11).

Among the clinical manifestations of hyperandrogenism, hirsutism was the most common. Similar results were reported by Najem et al. (9) where hirsutism was reported in 90.8% of patients. Acanthosis nigricans and acne in Najem et al study were similar to our study, 15.8%, and 12% respectively. In contrast, Amato et al. (12) documented a lower

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prevalence of hirsutism (57.7%).

Menstrual disturbances were also prevalent; oligomenorrhea was observed in 81% of patients in this study. Comparable results were reported by Najem et al. (9), who found oligomenorrhea in 85.8% of PCOS patients. Ultrasound evaluation revealed features consistent with PCOS was lower than that reported in studies using transvaginal ultrasound (96.7%), likely due to the lower sensitivity and higher operator dependency of transabdominal ultrasound (13,14). Thyroid disorders identified among third of the participants, autoimmune hypothyroidism was the most prevalent. According to prior reports, anti-thyroid antibodies and elevated TSH presented in 27% and 11% of PCOS patients, respectively (15). The prevalence of autoimmune hypothyroidism was 22.1% in Arduc et al. study (16), which was higher than our study. Sinha et al. (17) compared 80 women with PCOS to 80 controls and observed a significantly higher prevalence of goiter (27.5% vs. 7.5%) and subclinical hypothyroidism (22.5% vs. 8.75%) among the PCOS group. As compared to Lubecka et al. (18) the prevalence of subclinical hypothyroidism ranged from 11.3% to 30.3% (mean, 20.3%) among patients with PCOS. Also, in Raj et al. (19) they found that subclinical hypothyroidism more prevalent in participant with PCOS compared to participants without PCOS (43.5% vs. 20.5%).

CONCLUSION

Overall, the prevalence of thyroid disorders among patients with PCOS was 31%; the main thyroid disorder was autoimmune thyroiditis.

LIMITATIONS

A retrospective study from a patients' files and some data might be missing.

RECOMMENDATION

It is recommended that all patients with PCOS undergo routine screening for thyroid function and thyroid-specific autoantibodies, even if clinical signs of thyroid disease are absent.

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Genetic Neuromuscular Diseases in Libya.

Heba Abdelrazik El-Zawawi [1*].

Letter to Editor

Dear Editor:

Whereas in previous decades the landscape for certain disorders such as cancer and genetic diseases, in particular neuromuscular, was bleak, a glimmer of hope has now arisen. This glimmer is growing fast into a beam that promises to shine light over the coming decades. Genetic therapy has finally arrived.

I wish to shed light on the prospects in our location here in Libya: what has been done so far and what remains to be done. Our experience over the last 4 years will also be outlined. The reader will find that we have much to be proud of, and yet the challenges have been sometimes seemingly insurmountable.

The scientific committee for genetic neuromuscular diseases (NMDs) was instituted in Libya four years ago. (1) Members include adult and pediatric neurologists' representatives from most of the main cities of Libya as well as legal, pharmacist, and administrative members. It is part of the Libyan Program for Neuromuscular Diseases, which includes the Patient Neuromuscular Society. Thus, Libya has made considerable progress in the promotion of patient advocacy for these conditions. The neurologist members of the scientific committee are the heads of subcommittees formed in the city or city location to which they belong. Thus, a network covering all of Libya has been formed. The main concept overriding this organization is teamwork. Patients attend the subcommittee clinics to be assessed, tested genetically, counselled, treated, and followed up. Accurate statistics can be obtained regarding these diseases' incidence and prevalence in Libya. A national patient database is now the next aim.

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GENETIC TESTING

Around 1052 patients had genetic testing, and from the results we found spinal muscle atrophy (SMA), Duchenne muscle dystrophy (DMD), and other NMDs, with limb girdle muscle dystrophy being the most prevalent (Figure 1). (1)

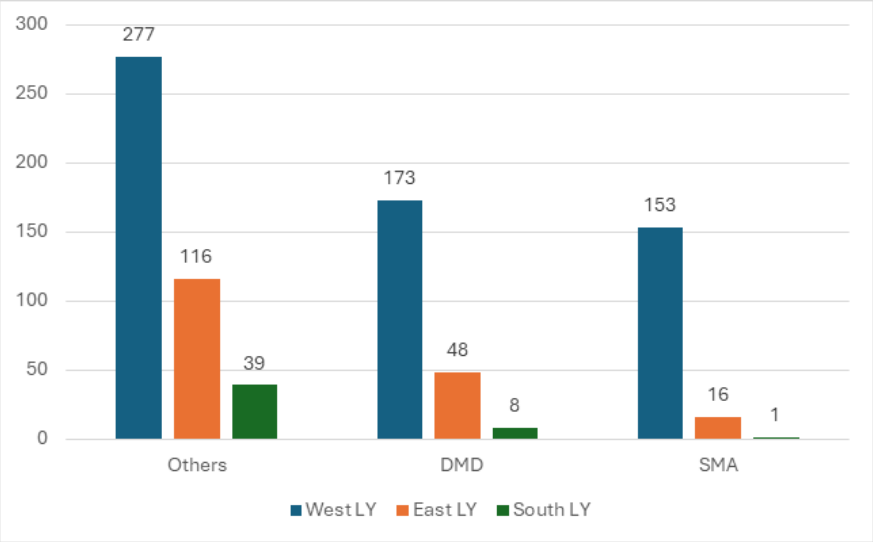

Figure 1: Genetic neuromuscular diseases in Libya 2022-2024.

Libya's Epidemiology for Genetic Neuromuscular Diseases:

We calculated the prevalence of SMA and DMD as 3.02/100,000 population and 7.06/100,000 males, respectively. (1)

With regard to SMA in particular, this was considered to be high as compared to the rest of the world and may be the result of consanguineous marriages in our location for this autosomal recessive disorder. This highlights the importance of prenatal genetic testing, neonatal screening, and family counselling and planning, especially in families with a history of genetic diseases. It is our hope to participate in a national program and campaign for genetic diseases, which would address all these aspects of diagnosis, prevention, and treatment where possible.

GENETIC THERAPIES:

The field of treatments for various genetic diseases is rapidly expanding; the mechanistic approaches include those for SMA. Nusinersen is an antisense oligonucleotide given intrathecally, and Risdiplam is a small DNA splicing protein that is given orally and is now freely available for SMA patients in Libya (around 150 patients). Gene therapy with Onasemnogene abeparvovec is given early to patients before age 2 years who weigh less than 21 kg and corrects the gene defect. An adenovirus vector carries a new gene into the patient's DNA to form the missing SMN protein. (2) It is a highly specialized treatment for which so far Libyan children have been sent to Egypt (18 patients) and, following that, to the United Arab Emirates (6 patients so far), where they received the therapy at specialized centers for genetic diseases. The treatment is now available to be given intrathecally for ages above 2 as well and higher weights. (3) The challenge for most health services will be meeting the cost of the expensive treatments.

Genetic therapies for Duchenne Muscle Dystrophies: include exon-skipping therapies with antisense oligonucleotides; 103 patients with appropriate gene mutations received their first doses of these intravenous therapies. (4) Ataluren was given to 40 patients with nonsense mutations but has been

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stopped pending FDA decision, as in a study it was found not to be sufficiently effective. (5) Luckily, givinostat, a histone deacetylase inhibitor, which has also been used in hematological conditions, (6) will soon become available for all patients with DMD who do not receive exon-skipping medications, around 200 patients. (7) Steroids are provided to all patients.

The plan is now to make gene therapy delandistrogene moxeparvovec-rokl available inside Libya for mobile patients with DMD. This therapy is with an adenovirus vector carrying a micro-dystrophin gene, which will be incorporated in the patient's DNA to form a functioning micro-dystrophin protein. It is approved for ambulatory individuals at least 4 years old with Duchenne muscular dystrophy (DMD) who have a confirmed mutation in the DMD gene. (8) The therapy will require intensive care and other specialized facilities as well as training of staff. We aim to collaborate with teams in the region who have experience in giving this therapy with success.

Vaccinations and Vaccination Campaigns:

The Scientific Committee provides guidelines and supervises programs that aim to cover all aspects of the genetic neuromuscular patients' daily life. Recently a national influenza vaccination program was organized.

The Multidisciplinary Team Concept:

This concept, although new in our health service, was readily adopted by the Scientific Committee, and although the challenge was and remains to provide such multiple specialty teams to all the major cities in Libya, the fact that treating physicians are now aware that patients must be approached holistically has been a great advancement in their care.

Social coverage and patient advocacy:

The plight of patients with neuromuscular disease in a developing country environment clearly reached all concerned, including the authorities and the Libyan public. A very close relationship exists between the patients, their families, and the Scientific Committee through the Libyan Neuromuscular Patient Group, which is a main stakeholder in the Libyan Program for Genetic Neuromuscular Diseases. Patients in Libya voice their concerns and state their individual as well as community requirements loudly, and they are heard. The Scientific Committee liaises with the government-funded departments concerned, including the Social Security Services, to ensure their needs are met. This is aimed at providing where needed BiPAP machines, cough assist devices, and electronic wheelchairs, as well as home adaptations and other necessities for the daily life of these patients.

Physiotherapy and rehabilitation:

The challenge was to provide specialized physiotherapy and rehabilitation services to all patients with these conditions all over Libya. Therefore, several training courses were arranged for physiotherapists locally and abroad, as well as a resident visiting specialist team from Slovakia. The visiting team provides both treatment for patients and training of local physiotherapists.

Surgery for Scoliosis: It is recognized that scoliosis is a debilitating complication of neuromuscular diseases, which, having been brought to the attention of our authorities, led to several visits by specialized surgical teams to perform corrective surgery in Libya and train Libyan surgeons to perform this surgery in the future. This surgery is performed under neurophysiological and radiological control, and therefore training in these specialties is also required.

Genetic treatment in Libya: The Future: The future aims to keep Libya in the mainstream of the rapidly advancing field of genetic discoveries, whether in testing and diagnosis or the development of effective new therapies. Adenovirus vector gene replacement is not the only mechanistic approach. CRISPR-Cas9-based therapies are also being considered and are in the pipeline. (9) We are likely to get therapies for other forms of genetic neuromuscular diseases such as limb girdle muscle dystrophies. In order to keep up, Libya must upgrade the health service, train specialists in genetics, and provide genetic laboratories and newborn screening, as well as genetic clinics where counselling can be given. We must also provide and equip multidisciplinary teams working in specialized centers and also promote and

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fund research.

CONCLUSION:

Libya is now considered a model state in North Africa for addressing the needs of patients with genetic neuromuscular diseases and funding genetic therapies for its patients. We have come a long way since these diseases were considered hopeless for patients, but there is still much more to be done.

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