

DISEASES

Primary Squamous Cell
Carcinoma of the Breast...

Testicular Filariasis – A Case
Report

Caregiver Stress in ESRD
Hemodialysis

Discovering Thoughts, Inventing Future

VOLUME 26 / ISSUE 1 / VERSION 1.0

**GLOBAL JOURNAL OF
MEDICAL RESEARCH**

Section F - Diseases

Volume 26

2026

Issue F1

Global Journal of Medical Research

ISSN (Online): 2249-4618 • ISSN (Print): 0975-5888

Open Access Policy

All articles published in Global Journal of Medical Research are open access articles published under the Global Journals Open Access Publishing Agreement, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Publisher

Global Journals Incorporated
301 Edgewater Place, Suite 100
Wakefield, MA 01880, United States

Copyright

© 2026 by Global Journals Incorporated (USA). All rights reserved.

No part of this publication may be reproduced or transmitted in any form or by any means, electronic or mechanical, including photocopy, recording, or any information storage and retrieval system, without written permission.

Disclaimer

The authors, editors, and publisher will not accept any legal responsibility for any errors or omissions that may be made in this publication. The publisher makes no warranty, express or implied, regarding the material contained herein.

Editorial Board

Global Journal of Medical Research

Antonio Simone Lagan

University of Messina, Italy

Caddie Laberiano

University of Texas, United States

Changlin Yang

University of Florida, United States

Dominik Lewandowski

University of California, United States

Dr. (Mrs.) Sunanda Sharma

Swami Keshwanand Rajasthan Agricultural University, India

Dr. Alfio Ferlito

University of Udine, Italy

Dr. Arpita Myles

United States

Dr. CHO Chi-Shing, William

Queen Elizabeth Hospital, Hong Kong

Dr. Feng Feng

Boston University, United States

Dr. Guodong Niu

Pennsylvania State University, United States

Dr. Han-Xiang Deng

Chinese Academy of Sciences, China

Dr. Hiroshi Suzuki

Niigata Seiryō University, Japan

Dr. Ivandro Soares Monteiro

University of Minho, Portugal

Dr. Izzet Yavuz

Dicle University, Turkey

Dr. KHUE VU NGUYEN

Université Louis Pasteur, United States

Dr. Krishna M Vukoti

Case Western Reserve University, United States

Dr. Lisa Koodie

University of Minnesota, United States

Dr. M. Alagar Raja

Jawaharlal Nehru Technological University, Hyderabad, India

Dr. Marcia Elson

Columbia University, United States

Dr. Naina Deshpande

Jawaharlal Nehru Technological University, Hyderabad, India

Dr. Osama Hasan Alali

University of Aleppo, Syrian Arab Republic

Dr. P. Umar Farooq Baba

Sher-i-Kashmir Institute of Medical Sciences, India

Dr. Pejdic Ana

University of Nis, United States

Dr. Pina C. Sanelli

State University of New York, United States

Dr. Rabiatul Basria SMN Mydin

Universiti Sains Malaysia, Malaysia

Dr. Rajeev Vats

The University of Dodoma, Tanzania

Dr. Roberto Sanchez

Rockefeller University, United States

Dr. Sanjay Dixit, M.D.

Cardiac Arrhythmia Univ of Penn School of Medicine, United States

Dr. Seung-Yup Ku

Seoul National University, South Korea

Dr. Sonia Jain

University of Calcutta, India

Dr. Subhadra Nandakumar

University of Madras, India

Dr. Tsvetelina Velikova

Sofia University "St. Kliment Ohridski", Bulgaria

Dr. Wael Ibrahim Abdo Aikhiary

Mansoura University, Egypt

Dr. Xingnan Li

Stanford University, United States

Dr. Yash Kapadia

University of Louisville, United States

Dr. Zhiming Li

Columbia University, United States

Hengrui Liu

University of Cambridge, United Kingdom

Ian Robertson

Uniformed Services University, United States

Maria Jose Pelaez Soni

Rice University, United States

Mojtaba Lashgari

University of Leeds, United Kingdom

Peter C. Hart

Roosevelt University, United States

Rama Rao Ganga

University of Health Sciences, United States

Sanguansak Rerksuppaphol

Srinakharinwirot University, Thailand

Shravan Gowrishankar

Cambridge University, United Kingdom

PREFACE

The Global Journal of Medical Research (GJMR) is pleased to present this issue, bringing together a curated collection of high-quality research papers that explore the latest advances in medical science and clinical practice.

This issue features research spanning topics including neurology, pharmacology & drug discovery, microbiology & pathology, radiology & diagnostics, gynecology, diseases, veterinary science, orthopedics, surgery & cardiovascular medicine, dentistry, nutrition, and interdisciplinary medical studies. Each paper has undergone a rigorous double-blind peer-review process to ensure clinical rigor and scientific originality.

We would like to express our sincere gratitude to the authors for entrusting their research with us, to the reviewers for their thorough and constructive evaluations, and to our readers for their continued engagement with the medical scientific discourse.

We hope that the research presented herein inspires further inquiry and contributes meaningfully to the advancement of medical knowledge and patient care.

The Chief Editor
Global Journal of Medical Research
Global Journals Organization

TABLE OF CONTENTS

Title	Author	Pages
Copyright		i
Editorial Board		ii
Preface		iv
Primary Squamous Cell Carcinoma of the Breast: Diagnostic Challenges and Therapeutic Insights From a Rare Case	Lombardi et al.	1-5
Testicular Filariasis – A Case Report	Aruna et al.	6-7
Evaluating Stress among Family Caregivers of Hemodialysis Patients with End-Stage Renal Disease	Chadayan et al.	7-13
Conceptual and Biological Inconsistencies in the Insulin Resistance Paradigm of Type 2 Diabetes	Poothullil	14-18
Multiple Myeloma with Unusual Hypopharyngeal Involvement: A Case Report	Briguglio	19-21
Subject Index		22
Author Guidelines		23



Primary Squamous Cell Carcinoma of the Breast: Diagnostic Challenges and Therapeutic Insights From a Rare Case

Article Record

Dr. Welington Lombardi^{§§*}
MD, PhD, Full Professor of Gynecology and Obstetrics
*Corresponding Author



Maria Clara Vieira Martinez^{§§}
Medical students



Isabella Franco Barbosa Pesce^{§§}
Medical students



Pietra Lopes Monti^{§§}
Medical students



Letícia Dalavale Fabretti^{§§}
Medical Residents in Gynecology and Obstetrics



Roseane Rigo^{§§}
Medical Residents in Gynecology and Obstetrics



Daniela Videira Botton^{§§}
Medical Residents in Gynecology and Obstetrics



Thais Luiza Pavan Martins^{§§}
Medical Residents in Gynecology and Obstetrics



§ Gynecology and Obstetrics, University of Araraquara, Araraquara, Brazil (OA)
+4 additional authors listed on the metadata continuation page.

RECEIVED

2026-01-29

ACCEPTED

2026-02-12

PUBLISHED

2026-04-04

PEER REVIEW

Double Blind

Abstract

Primary squamous cell carcinoma (SCC) of the breast is a rare type of cancer, representing between 0.06% and 0.2% of malignant breast tumours. The disease presents with rapid growth and an aggressive pattern, and the lack of well-defined therapeutic protocols hinders its treatment. The following is a case report of a 64-year-old female patient presenting with a large nodule in her left breast (>10 cm) with rapid and progressive growth and palpable ipsilateral axillary lymph nodes. The histopathological examination of the core biopsy of the lesion showed a poorly differentiated carcinoma and was clinically staged as an inflammatory carcinoma (T4d N1 Mx). The patient was referred for neoadjuvant chemotherapy with paclitaxel and carboplatin, but showed a poor response with tumor progression, and was referred for hygienic mastectomy surgery. The histopathological result of the surgical specimen showed an invasive carcinoma with squamous differentiation, grade 3, ulcerated, with invasion of the pectoralis muscle and free margins (pT4b pNx pMx). Only after immunohistochemistry of the surgical specimen was it possible to confirm the definitive diagnosis of keratinising squamous cell carcinoma (SCC). Postoperatively, the patient returned with signs of surgical wound dehiscence and pleuropulmonary and mediastinal metastatic progression. After multidisciplinary and family discussion, exclusive palliative care was instituted. Primary squamous cell carcinoma (SCC) of the breast typically manifests rapidly and aggressively, and its diagnosis is quite challenging, requiring histopathological confirmation and, primarily, immunohistochemistry. The gold standard treatment includes breast surgery with clear margins, but there is no consensus regarding adjuvant chemotherapy. Its prognosis is usually guarded, especially in locally advanced or metastatic cases.

Primary squamous cell carcinoma

breast cancer

keratinizing carcinoma

metaplastic breast tumor

aggressive breast neoplasm

neoadjuvant chemotherapy

mastectomy

AI USE STATEMENT

No generative AI was used for analysis or results.

FUNDING

No external funding was declared for this work.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

DATA AVAILABILITY

Not applicable for this article.

ETHICS

No ethics committee approval was required for this article type.

CONSENT

Not applicable for this article.

TRIAL REG.

Not applicable.

Crossref DOI: 10.34257/GJMRFVOL26IS1PG1

How to Cite: Lombardi et al. (2026). Primary Squamous Cell Carcinoma of the Breast: Diagnostic Challenges and Therapeutic Insights From a Rare Case. Global Journal of Medical Research, 26(1), 1-5. DOI: 10.34257/GJMRFVOL26IS1PG1

LICENSE

© 2026 Global Journals. Open-access article under CC BY-NC-ND 4.0 International License.

METADATA CONTINUATION

AUTHOR CONTACT QR LEDGER

Dr. Welington Lombardi§0*		Maria Clara Vieira Martinez§§		Isabella Franco Barbosa Pesce§§		Pietra Lopes Monti§§	
Leticia Dalavale Fabretti§0		Roseane Rigo§0		Daniela Videira Botton§0		Thais Luiza Pavan Martins§0	
Vitória Ribeiro Farinha§0		Carla de Freitas§II		Flávia Vicentin Silva§II		Luciana Borges Lombardi§II	

COMPLETE AUTHOR LEDGER

01. Dr. Welington Lombardi §* | 0 MD, PhD, Full Professor of Gynecology and Obstetrics | Gynecology and Obstetrics, University of Araraquara, Araraquara, Brazil
02. Maria Clara Vieira Martinez § | § Medical students | University of Araraquara, Araraquara, Brazil
03. Isabella Franco Barbosa Pesce § | § Medical students | University of Araraquara, Araraquara, Brazil
04. Pietra Lopes Monti § | § Medical students | University of Araraquara, Araraquara, Brazil
05. Leticia Dalavale Fabretti § | 0 Medical Residents in Gynecology and Obstetrics | Gynecology and Obstetrics, University of Araraquara, Araraquara, Brazil
06. Roseane Rigo § | 0 Medical Residents in Gynecology and Obstetrics | Gynecology and Obstetrics, University of Araraquara, Araraquara, Brazil
07. Daniela Videira Botton § | 0 Medical Residents in Gynecology and Obstetrics | Gynecology and Obstetrics, University of Araraquara, Araraquara, Brazil
08. Thais Luiza Pavan Martins § | 0 Medical Residents in Gynecology and Obstetrics | Gynecology and Obstetrics, University of Araraquara, Araraquara, Brazil
09. Vitória Ribeiro Farinha § | 0 Medical Residents in Gynecology and Obstetrics | Gynecology and Obstetrics, University of Araraquara, Araraquara, Brazil
10. Carla de Freitas § | II Medical Specialists in Mastology | University of Araraquara, Araraquara, Brazil
11. Flávia Vicentin Silva § | II Medical Specialists in Mastology | University of Araraquara, Araraquara, Brazil
12. Luciana Borges Lombardi § | II Medical Specialists in Mastology | University of Araraquara, Araraquara, Brazil

ARCHIVAL RECORD

Primary Squamous Cell Carcinoma of the Breast: Diagnostic Challenges and Therapeutic Insights From a Rare Case

Dr. Welington Lombardi^{§*}, Maria Clara Vieira Martinez^{§ξ}, Isabella Franco Barbosa Pesce^{§ξ}, Pietra Lopes Monti^{§ξ}, Leticia Dalavale Fabretti^{§θ}, Roseane Rigo^{§θ}, Daniela Videira Botton^{§θ}, Thais Luiza Pavan Martins^{§θ}, Vitória Ribeiro Farinha^{§θ}, Carla de Freitas^{§II}, Flávia Vicentin Silva^{§II}, and Luciana Borges Lombardi^{§II}

Affiliations

§ Gynecology and Obstetrics, University of Araraquara, Araraquara, Brazil (OA)

Qualifications / Designations

§ MD, PhD, Full Professor of Gynecology and Obstetrics

ξ Medical students

θ Medical Residents in Gynecology and Obstetrics

II Medical Specialists in Mastology

Abstract

Primary squamous cell carcinoma (SCC) of the breast is a rare type of cancer, representing between 0.06% and 0.2% of malignant breast tumours. The disease presents with rapid growth and an aggressive pattern, and the lack of well-defined therapeutic protocols hinders its treatment. The following is a case report of a 64-year-old female patient presenting with a large nodule in her left breast (>10 cm) with rapid and progressive growth and palpable ipsilateral axillary lymph nodes. The histopathological examination of the core biopsy of the lesion showed a poorly differentiated carcinoma and was clinically staged as an inflammatory carcinoma (T4d N1 Mx). The patient was referred for neoadjuvant chemotherapy with paclitaxel and carboplatin, but showed a poor response with tumor progression, and was referred for hygienic mastectomy surgery. The histopathological result of the surgical specimen showed an invasive carcinoma with squamous differentiation, grade 3, ulcerated, with invasion of the pectoralis muscle and free margins (pT4b pNx pMx). Only after immunohistochemistry of the surgical specimen was it possible to confirm the definitive diagnosis of keratinising squamous cell carcinoma (SCC). Postoperatively, the patient returned with signs of surgical wound dehiscence and pleuropulmonary and mediastinal metastatic progression. After multidisciplinary and family discussion, exclusive palliative care was instituted. Primary squamous cell carcinoma (SCC) of the breast typically manifests rapidly and aggressively, and its diagnosis is quite challenging, requiring histopathological confirmation and, primarily, immunohistochemistry. The gold standard treatment includes breast surgery with clear margins, but there is no consensus regarding adjuvant chemotherapy. Its prognosis is usually guarded, especially in locally advanced or metastatic cases.

Keywords: Primary squamous cell carcinoma, breast cancer, keratinizing carcinoma, metaplastic breast tumor, aggressive breast neoplasm, neoadjuvant chemotherapy, mastectomy, histopathology, immunohistochemistry

* Corresponding Author

Dr. Welington Lombardi

DOI

10.34257/GJMRVOL26IS1PG1

1. Introduction

Non-melanoma skin cancer is a significant public health problem, with an incidence increasing by 4% to 8% annually in developing countries¹. Of new cancer cases registered, approximately 20% are located in the skin, making it the most frequent type of cancer in the world². Primary squamous cell carcinoma (SCC) of the breast is considered a very rare malignant neoplasm, with an estimated prevalence between 0.06% and 0.2% of breast neoplasms^{2,3}. Its occurrence is not well established, but it may be related to squamous metaplasia of the ductal epithelium or even originate from alterations during embryonic development⁴. Squamous cell carcinoma (SCC) presents rapid progression and a high invasive and metastatic potential when compared to basal cell carcinoma. Because it is an extremely rare neoplasm in the breast region, its clinical diagnosis becomes challenging².

According to the literature, the prevalence of SCC is associated with white women, ranging from 52 to 64 years of age³. Pure

squamous cell carcinoma of the breast can originate from the epidermis, nipple, or even the epithelium of a deep epidermoid cyst or squamous metaplasia⁵. When it occurs in the breasts, the lesion can mimic breast cancer, with a desquamative and erythematous clinical presentation, of an irregular and verrucous lesion². It is classified by the World Health Organisation (WHO) as a specific and distinct subtype of metaplastic tumour and presents the following criteria: 90% or more of the lesion composed of keratinising squamous cell carcinoma infiltrating mammary parenchyma; absence of other invasive neoplastic elements; no extensive involvement of the skin overlying the tumour and absence of primary neoplastic skin lesions³.

In addition to its rarity, this carcinoma generally has a poor prognosis due to its aggressive nature and the lack of specific treatments, as there is no established protocol for it³. Core biopsy and immunohistochemistry are used for its diagnosis⁴. Any lesion that presents a clinical suspicion should be rigorously evaluated,

with early biopsy requested to ensure an accurate diagnosis and avoid unnecessary radical therapies².

Regarding treatment, there is no consensus on the best clinical approach, but chemotherapy remains one of the options used. The chemotherapy regimen with cisplatin and fluorouracil has been described as an excellent option, with reasonable responses reported after its use⁴. However, surgical removal of the lesion remains the treatment of choice (gold standard), as it allows for complete histopathological examination of the tumour, evaluation of surgical margins, and assessment of prognostic factors such as perineural invasion. In cases of excision of small tumors, where the surgical margins are clear, i.e., 4 mm to 10 mm from the lesion, the cure rate is estimated at almost 99%².

Therapeutic approaches should be analysed and planned on a case-by-case basis, taking into account the patient's particular factors and preferences. Advanced cases of breast squamous cell carcinoma (SCC) may require mastectomy with axillary lymphadenectomy combined with adjuvant chemotherapy. However, in cases of primary breast SCC, removal with wide surgical excision is recommended, with lymph node dissection only necessary when there is clinical evidence of axillary spread. Histopathological confirmation, along with immunohistochemical evaluation and clinical history, is fundamental for the correct diagnosis of this rare type of tumour².

Therefore, the rarity of this case, its diagnostic difficulty, and the uncertainties regarding the best treatment to be instituted justify the writing of this article.

2. Case Report

Female patient, 64 years old, black race, G3P3C0A0, menarche at age 15, menopause at age 53, with no prior use of hormone replacement therapy. She reported being a chronic smoker, with no other reported comorbidities or relevant family history.

The patient was referred to the Mastology Service with a history of a palpable nodule in the left breast, associated with progressive growth. On physical examination, the left breast was larger than the right, due to a large nodule in the left breast, measuring more than 10 cm, associated with an ulcerated lesion, local skin thickening, and the presence of palpable lymph nodes in the ipsilateral axillary region (Figure 1).

Regarding the complementary exams, the patient brought a recent mammogram, classified as BIRADS 3 (Breast Imaging Reporting and Data System), which described a solid, hypoechoic, oval nodule with circumscribed margins, located at the junction of the medial quadrants of the left breast, measuring 4,5 x 4,0 x 4,3 cm.

In light of the clinical findings, a core biopsy of the lesion guided by ultrasound was requested, whose anatomopathological examination revealed a poorly differentiated, solid carcinoma. Immunohistochemistry revealed a triple-negative pattern, with negative estrogen receptor (ER), progesterone receptor (PR), and human epidermal receptor (HER2) and a proliferation antigen (Ki-67) of 70%.



Figure 1. Physical examination showing a large tumor lesion in the left breast, with significant distension and ulceration of the skin, with associated secretion.

Source: author's own.

The chest CT scan showed a small solid subpleural nodule in the posterior basal segment of the left lower lobe, measuring 0.7 x 0.7 cm, suggestive of secondary pleuropulmonary involvement. Breast ultrasound showed a heterogeneous nodular formation, difficult to measure, occupying the entire left mammary parenchyma, associated with the presence of ipsilateral axillary lymphadenopathy, measuring 2.6 x 1.2 cm, which is atypical. Both bone scintigraphy and abdominal tomography were negative for secondary lesions.

Due to the size of the lesion, the patient was referred to the Oncology Service for neoadjuvant chemotherapy. Treatment with

paclitaxel and carboplatin was chosen because this combination is widely recommended and used in advanced cases of breast and gynecological neoplasms and, as neoadjuvant chemotherapy, significantly increases the complete pathological response. However, after four cycles with this weekly protocol, the patient showed a poor response and significant tumour progression and was then submitted to hygienic mastectomy surgery.

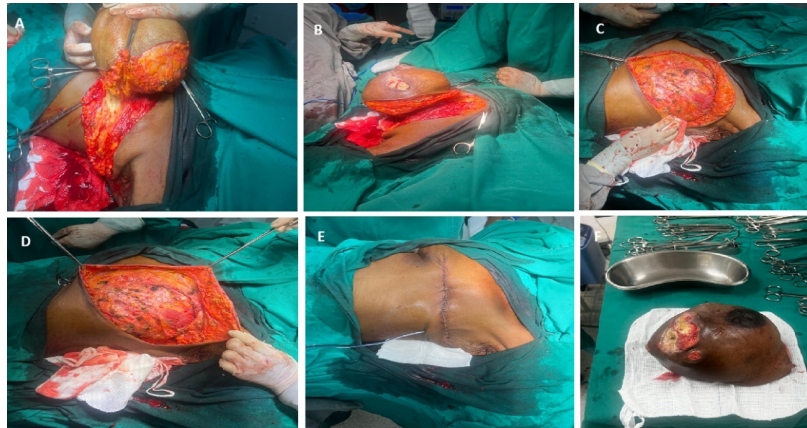


Figure 2. Radical mastectomy of the left breast, Halsted type (A, B and C). Intercostal muscle, without the pectoralis major muscle, is already excised (D). Final closure with skin suture and Portovac drain (E). Final view of the surgical specimen (left breast).

Source: author's own.

The histopathological examination revealed invasive carcinoma with squamous differentiation, ulcerated, grade 3, measuring 17.0 x 12.0 x 10.0 cm, with focal angiolymphatic invasion, infiltration of the pectoral muscle and free margins (pT4b pNx pMx) (Figure 3).

Diagnostic Conclusion		
Left Breast:		
Invasive carcinoma with squamous cell differentiation, ulcerated		
Histological Grade (Scarff-Bloom-Richardson modified by Elston and Ellis): Poorly Differentiated \ Grade 3		
Mitotic Index: 22 mitoses \ 10 CGA		
Tumor Size: 17,0 x 12,0 x 10,0 cm		
Angiolymphatic Invasion: Present		

Figure 3. Histopathological examination of the surgical specimen showed invasive carcinoma with Ulcerated Squamous Cell Differentiation.

Source: author's own.

Only after performing immunohistochemistry on the surgical specimen was the diagnosis of keratinising squamous cell carcinoma (SCC) definitively confirmed (Figure 4).

marcador		
antígeno	clone	resultado
AE1/AE3	AE1/AE3	positiva
CK5-6	D5/16 B4	positiva difusamente
GATA3	L50-823	positiva fraca e focal
HER2	4B5	negativa 1+/3 (escore 1+ / imunoeexpressão pouco perceptível, membrana incompleta, em 15% das células neoplásicas)
Ki-67(30-9)	30-9	positiva em 60% das células
P63	4A4	positiva
RE (SP1)	SP1	negativa
RP (1E2)	PGR 636	negativa
SOX-10	EP268	negativa
conclusão		
painel imuno-histoquímico, associado aos aspectos histológicos, de:		
- Carcinoma de células escamosas, queratinizante, infiltrativo em tecido fibroadiposo (vide comentário).		

Figure 4. Immunohistochemistry panel confirming the diagnosis of keratinising squamous cell carcinoma.

Source: author's own.

In the immediate postoperative period, the patient developed dehiscence of the surgical wound, in addition to disease progression in the anterior mediastinum and pleura. The case was discussed with the Clinical Oncology and Radiotherapy teams, and it was decided to perform palliative radiotherapy in the anterior hemithorax, followed by capecitabine as a second-line treatment. Upon conducting a new chest CT scan for therapeutic planning, a mass was found in the sternal region, with a significant increase in tumour volume. The adoption of exclusive palliative care was discussed with the patient and her family, and it was agreed that no further interventions would be performed.

3. Discussion

Primary squamous cell carcinoma of the breast is very rare, with a prevalence of 0.06% to 0.2% in malignant breast neoplasms^{2,3}. It is called primary pure squamous cell carcinoma when the malignant cells are all of the squamous cell type, there is no relation with the skin, and if there is no indication for a primary location somewhere else in the body⁵. Furthermore, it has a rapid and aggressive course, with a recurrence rate of 25% and metastasis in 50% of cases^{3,6}. SCC typically progresses rapidly and is highly invasive, most frequently found on exposed body surfaces most frequently seen in the sun and is uncommon in the breasts².

For a more accurate diagnosis, it is essential to differentiate between squamous cell carcinoma (SCC) of the skin and primary squamous cell carcinoma of the breast, which differ in their epidemiology and histopathology. The former is more prevalent in black individuals and in males, and its most common clinical manifestation is an erythematous-squamous or slightly raised plaque. Furthermore, it can present as an ulcerated lesion with irregular borders or as an exophytic nodular lesion, similar to that presented in the case described⁶. The latter is prevalent in white women and may originate from the epidermis, nipple, or even the epithelium of a deep epidermoid cyst or squamous metaplasia^{3,5}. It is important to distinguish this type from mixed tumours, where some patches of squamous cells can be found in adenocarcinoma of the breast and from metastasis of squamous cell carcinoma that originated elsewhere. The etiology and pathogenesis of squamous cell carcinoma of the breast is still unclear. It has been suggested that it may be a very extreme form of squamous cell metaplasia, developing into an adenocarcinoma⁷.

The clinical presentation may be painful breast inflammation or a tumor that is always larger than that of breast adenocarcinoma, similar to that found in the case described⁸.

Regarding imaging studies, there are no typical findings on mammography, and ultrasound may show a complex cyst or an inflammatory process⁵. In our case, mammography showed only one solid, hypoechoic nodule with circumscribed margins, located at the junction of the medial quadrants of the left breast, measuring 4,5 cm. The patient did not undergo breast ultrasound. It is still debatable whether investigations such as PET scans, in search of distant metastases or a primary squamous tumour site, should be performed⁹.

For a more precise diagnosis, a core needle biopsy should be performed, as it provides a greater amount of material (tissue) to be analysed⁶. Regarding the diagnosis, immunohistochemical examination should always be performed, as it allows confirmation of the squamous nature of the tissue and differentiation from other types of breast carcinomas, such as metaplastic carcinoma⁵. This differentiation is of great importance, as primary squamous cell

carcinoma of the breast behaves more aggressively than other breast cancers⁵.

Squamous cell carcinoma of the breast may require surgery with wide excision to obtain clear margins, as occurred in the reported case². Regarding lymph node dissection, it should only be indicated when there are signs of axillary invasion, either clinically or by ultrasound².

Treatment is not specific due to the lack of an established protocol; however, one possible treatment involves adjuvant hormonal therapy with tamoxifen, which is essential when patients are positive for estrogen and progesterone receptors³. Squamous cell carcinomas are generally hormone receptor-negative^{8,10}. For patients with negative expression of these receptors, conventional chemotherapy is necessary, as used in the aforementioned case⁵.

Postoperative chemotherapy should be recommended and, similar to other cases reported in the literature, the combination of paclitaxel and carboplatin appears to be the best option currently⁵. This chemotherapy regimen is used in advanced cases of breast, ovarian, and lung cancer. Both cisplatin and carboplatin interact with DNA, inhibiting cell growth (paclitaxel) and damaging tumor DNA (carboplatin), with a high rate of pathological complete response when used in neoadjuvant chemotherapy¹¹. They have a mechanism of action similar to bifunctional alkylating agents, destroying rapidly dividing tumor cells¹².

Regarding radiotherapy, it is recommended to administer it as adjuvant therapy, however the radiosensitivity of squamous cell carcinomas is still uncertain. The 5-year survival rate is around 67%¹³.

Therefore, primary squamous cell carcinoma of the breast is an uncommon finding. Its existence and possible evolution from an apparently benign lesion remain uncertain. For its definitive diagnosis, we emphasize the importance of histopathological examination and immunohistochemistry. Regarding treatment, the role of surgery is well established, but the role of adjuvant therapy is not yet well defined⁵.

In this particular case, the patient began treatment with neoadjuvant chemotherapy, showing a poor response with disease progression, and subsequently underwent radical breast surgery due to the size of the initial lesion, with clear surgical margins. Despite all the treatment instituted and due to the aggressive nature of the neoplasm, the patient soon experienced significant mediastinal recurrence, considered inoperable, and was referred for palliative and supportive care.

■ REFERENCES

- [1] Pătrașcu, V. *et al.* Histopathological and clinical-progressive profile of skin carcinomas: study on 1688 cases. **Romanian Journal of Morphology and Embryology**. [S.L.], v. 51, n. 1, p. 171-180, 2010. Available at: https://www.researchgate.net/profile/Virgil-Patrascu/publication/41623720_Histopathological_and_clinical-progressive_profile_of_skin_carcinomas_Study_on_1688_cases/links/0912f5023dbef510d1000000/Histopathological-and-clinical-progressive-profile-of-skin-carcinoma-s-Study-on-1688-cases. Accessed on: October 28, 2025.
- [2] Melo Neto, B. *et al.* Epidermoid carcinoma of the skin mimicking breast cancer: case report. **Anais Brasileiros de Dermatologia**. [S.L.], v. 88, n. 2, p. 250-252, 2013. Available at: <https://www.scielo.br/j/abd/a/Bn4sZTxRRSQYghkf6W8V/FDC/?lang=en>. Accessed on: October 28, 2025.

- [3] Cardoso L. G. F. *et al.* Metaplastic squamous cell carcinoma of the breast: a case report and literature review. **Archives of Health**. v. 5, n. 3, p. 01-06, 2024. Available at: <https://ojs.latinamericanpublicacoes.com.br/ojs/index.php/ah/article/view/208>. Accessed on August 11, 2025.
- [4] Pereira R. J. *et al.* Squamous cell carcinoma of the breast: a case report. **Brazilian Journal of Gynecology and Obstetrics**. v. 21, n. 7, 1999. Available at: <https://www.scielo.br/r/jrbgo/a/f4XHtr6CVJvww7DMzC6Ytky/?format=html&lang=pt>. Accessed on August 11, 2025.
- [5] Bhosale S.J. *et al.* Squamous cell carcinoma of the breast. **American Journal of cases reports**. [S. l.] v. 14, p. 188-190, 2013. Available at: <https://amjcaserep.com/abstract/full/idArt/883934>. Accessed on August 11, 2025.
- [6] Ortiz, J. *et al.* Primary squamous cell carcinoma of the breast: a case review. **CIMEL Ciencia e Investigación Médica Estudiantil Latinoamericana**. v.12 n. 2, 2007. Available at: <https://www.redalyc.org/pdf/717/71712210.pdf>. Accessed on: September 8, 2025.
- [7] Stevenson JT, Graham DJ, Khiyami A, Mansour EG. Squamous cell carcinoma of the breast: a clinical approach: *Ann Surg Oncol*, 1996; 4; 367-74, pmid: 8790849.
- [8] Gupta G, Malani AK, Weigand RT, Rangenini G. Pure primary squamous cell carcinoma of the breast: A rare presentation and clinicopathologic comparison with usual ductal carcinoma of the breast: *Pathol Res Pract*, 2006; 6; 465-69, pmid: 16497446.
- [9] Healy CF, Feeley L, Leen E, Walsh TN. Primary squamous cell carcinoma of the breast: value of positron emission tomography scanning in confirming the diagnosis: *Clin Breast Cancer*, 2006; 5; 413-15, pmid: 17239268.
- [10] Siegelmann-Danieli N, Murphy TJ, Meschter S. Primary pure squamous cell carcinoma of the breast: *Clin Breast Cancer*, 2005; 3; 270-72, pmid: 16137440.
- [11] Perez EA, Hartmann LC. Paclitaxel and carboplatin for advanced breast cancer. *Semin Oncol*. 1996 Oct;23(5 Suppl 11):41-5. PMID: 8893899.
- [12] Cancer Research UK. Paclitaxel and carboplatin (PC, Carb-oTaxol). Available at: <https://www.cancerresearchuk.org/about-cancer/treatment/drugs/pc-paclitaxel-carboplatin>. Last reviewed: January 17, 2025. Accessed on: February 7, 2026.
- [13] Behranwala KA, Nasiri N, Abdullah N. Squamous cell carcinoma of the breast: clinico-pathologic implications and outcome: *Eur J Surg Oncol*, 2003; 29; 386-89, pmid: 12711295.



Testicular Filariasis – A Case Report

Article Record

DR.P.Aruna^{§*}
Assistant Professoe
ORCID 0009-0005-9609-5124
*Corresponding Author



Abhilasha Wahne^{§§}
Senior resident

Jeewan verma^{‡θ}
Assistant Professor

Anil kumar Verma^{§θ}
Assistant Professor

§ Pathology & Labmedicine, All India Institute of Medical Sciences Raipur, Raipur, India (OA)
‡ Department of General surgery, All India Institute of Medical Sciences Raipur, Raipur, India (OA)

RECEIVED
2026-02-11

ACCEPTED
2026-02-18

PUBLISHED
2026-04-04

PEER REVIEW
Double Blind

Abstract

Filariasis is a parasitic infection endemic to tropical and subtropical regions. The disease primarily affects the body's lymphatic system. In India, heavily infected areas with filariae are found in Orissa, Uttar Pradesh, Bihar, Andhra Pradesh, Tamil Nadu, Kerala, and Gujarat.[1]Genital filariasis in India more commonly presents as a secondary vaginal hydrocele with an associated epididymo-orchitis.[2] While testicular involvement is rare, the clinical manifestations of filariasis vary from person to person, depending on the course of infection and the worm load. It is very uncommon to find an adult worm in the testis.

Filariasis

Testis

Hydrocele

Torsion

AI USE STATEMENT

No generative AI was used for analysis or results.

FUNDING

No external funding was declared for this work.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

DATA AVAILABILITY

Not applicable for this article.

ETHICS

No ethics committee approval was required for this article type.

CONSENT

Not applicable for this article.

TRIAL REG.

Not applicable.

Crossref DOI: 10.34257/GJMRVOL26IS1PG5

How to Cite: Aruna et al. (2026). Testicular Filariasis – A Case Report. Global Journal of Medical Research, 26(1), 6-7. DOI: 10.34257/GJMRVOL26IS1PG5

LICENSE

© 2026 Global Journals. Open-access article under CC BY-NC-ND 4.0 International License.



Print ISSN 0975-5888



9 770975 588001

Online ISSN 2249-4618



9 772249 461010

Under the strict compliance and defined process of



METADATA CONTINUATION

AUTHOR CONTACT QR LEDGER

DR.P.Aruna\$0*



ARCHIVAL RECORD

Testicular Filariasis – A Case Report

DR.P.Aruna^{§*}, Abhilasha Wahne[§], Jeewan verma[‡], and Anil kumar Verma[§]

Affiliations

[§] Pathology & Labmedicine, All India Institute of Medical Sciences Raipur, Raipur, India (OA)
[‡] Department of General surgery, All India Institute of Medical Sciences Raipur, Raipur, India (OA)

Qualifications / Designations

[§] Assistant Professoe
^ξ Senior resident
^θ Assistant Professor

Abstract

Filariasis is a parasitic infection endemic to tropical and subtropical regions. The disease primarily affects the body's lymphatic system. In India, heavily infected areas with filariae are found in Orissa, Uttar Pradesh, Bihar, Andhra Pradesh, Tamil Nadu, Kerala, and Gujarat.[1]Genital filariasis in India more commonly presents as a secondary vaginal hydrocele with an associated epididymo-orchitis.[2] While testicular involvement is rare, the clinical manifestations of filariasis vary from person to person, depending on the course of infection and the worm load. It is very uncommon to find an adult worm in the testis.

Keywords: *Filariasis, Testis, Hydrocele, Torsion*

* Corresponding Author

DR.P.Aruna

DOI

10.34257/GJMRVOL26IS1PG5

Key Clinical Message

A 21 year old male presented with Right hydrocele with pain in Right hemi scrotum which was diagnosed clinically and radiologically as torsion and subjected to orchidectomy. Histopathology revealed filariasis. The case has been presented for its rarity.

of hemorrhage and necrosis, adult filarial worm surrounded by dense inflammatory cell infiltration of neutrophils, lymphoplasmocytes, and eosinophils were seen. No significant pathology was detectable in the epididymis or spermatic cord. A histopathological diagnosis of right-sided filarial orchitis was given.

1. Introduction

Filariasis is a parasitic infection endemic to tropical and subtropical regions. The disease primarily affects the body's lymphatic system. In India, heavily infected areas with filariae found in Orissa, Uttar Pradesh, Bihar, Andhra Pradesh, Tamil Nadu, Kerala, and Gujarat. [1] Genital filariasis in India more commonly presents as a secondary vaginal hydrocele with an associated epididymo-orchitis. [2] While testicular involvement is rare, the clinical manifestations of filariasis vary from person to person, depending on the course of infection and the worm load. It is very uncommon to find adult worm in the testis.

2. Case History

A 21-year-old young man presented with a history of pain and swelling in the Right hemiscrotum for 3–4 days with a history of trauma to scrotal area due to a fall 7–8 days back.

On examination, a tense cystic swelling of Rt hemiscrotum, firm in consistency, and a firm cord in consistency were found. USG examination of Rt testis was done and reported as Rt hematocele with Rt testicular torsion.

3. Treatment and Histopathology

Patient underwent a right orchiectomy. The specimen was sent for histopathological examination in 10% formalin. On examination, the entire right testis was dark brown. Histopathological examination showed a scanty rim of testicular tissue with extensive area

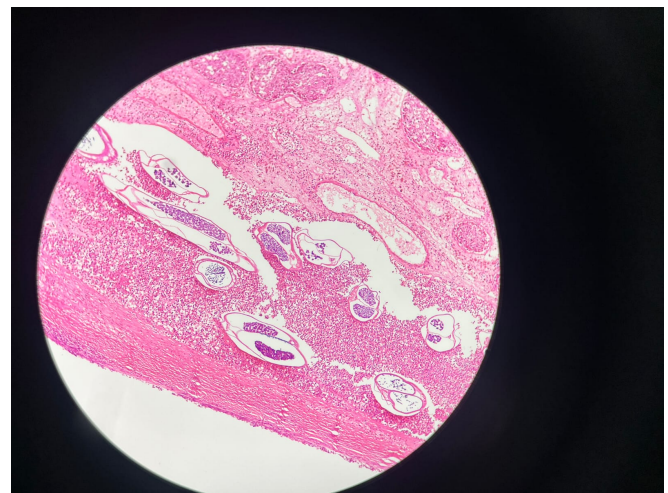


Figure 1. Female adult filarial worm in testicular parenchyma (H&E stain, 100X)

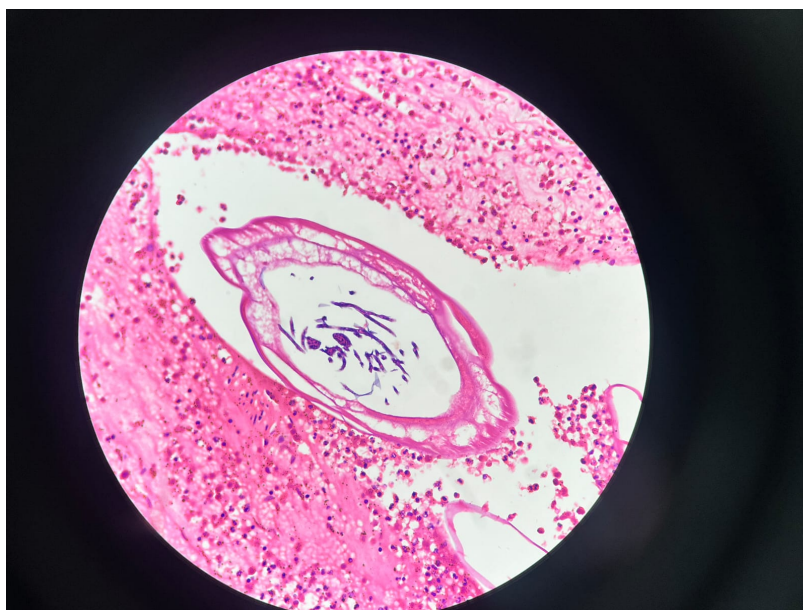


Figure 2. Double-barrel uterus of female adult filarial worm with microfilariae seen against the background of mixed inflammatory infiltrate (H&E stain, 400X)

4. Discussion

The filarial orchitis simulates grossly with neoplastic and non-neoplastic testicular and paratesticular lesions that include non-specific orchitis, tuberculous epididymo-orchitis, malignant mesothelioma, adenomatoid tumors, mesothelioma cyst and reactive mesothelioma hyperplasia, malakoplakia, sarcoidosis, and inflammatory pseudotumor. [3]

The filarial infection is prevalent in both urban and rural areas. Adult worms are found in the lymphatic vessels and lymph nodes of humans only; there is no animal reservoir. Adult worms in the lymphatic channels produce clinical manifestations of the disease due to lymphatic dysfunction, obstruction, and inflammation. Genital bancroftian filariasis may manifest in several ways including hydrocoele, lymph varix, lymph scrotum, filarial penis or elephantiasis of the genitalia, and chyluria. Hydrocoele accounts for 90% of the morbidity due to genital filariasis. Diagnosis of genital filariasis can be confirmed by direct demonstration of microfilaria in blood or aspirated fluid unequivocally. The tools available for the detection of active infection in an amicrofilaremic patient are circulating filarial antigen (CFA) tests and ultrasound with a high-frequency probe showing filaria dance sign (FDS). [4] This case report highlights an unusual presentation of genital filariasis where intense congestion of the testis and epididymis with microfilaria resulted in acute scrotum masquerading as testicular torsion.

5. Conclusion

Filarial orchitis may simulate clinically with many neoplastic and non-neoplastic lesions. The various differential diagnoses must be kept in mind when dealing with testicular swellings, especially in endemic areas, to avoid unnecessary orchidectomy.

■ AUTHOR CONTRIBUTION

All the authors contributed equally to the preparation of this manuscript.

■ CONSENT

Written informed consent could not be obtained in this case as the patient was lost to follow-up. Institutional ethical committee approval was obtained after declaring that the case report does not contain any patient identifiers.

■ REFERENCES

- [1] Park KP. Textbook of preventive and social medicine. 22nd ed. Jabalpur: Banarsidas Bhanot; 2013. p. 245–251.
- [2] Garg PK, Bhatt S, Kashyap B, George A, Jain BK. Genital filariasis masquerading as testicular torsion. *J Vector Borne Diseases*. 2011;48:119–121.
- [3] Barreto SG, Rodrigues J, Pinto RGW. Filarial granuloma of the testicular tunic mimicking a testicular neoplasm: a case report. *Journal of Medical Case Reports*. 2008;2:321.
- [4] Chaubal NG, Pradhan GM, Chaubal JN, Ramani SK. Dance of live adult filarial worms is a reliable sign of scrotal filarial infection. *J Ultrasound Med*. 2003;22:765–9.
- [5] Ranjan R, Choubey D, Kumar P, Besra RC, Sahu SS, Baxla RG, et al. Filarial Scrotal Tumour. *Journal of Evolution of Medical and Dental Sciences*. 2003;2(18):3171–3174.
- [6] Shyamkumar N, Mehrotra S, Athyal RP, Taranath A, Nair S, Govil S, Chacko NK. Can we see microfilaria on ultrasound? A real-time ultrasound and wet smear demonstration of dancing microfilaria. *The Internet J Urol*. 2004;2(1).
- [7] Hindi SAL, Asghar M, Hassan AA. Epididymal Filariasis in a Child. *Bahrain Medical Bulletin*. 2003;25:4.



Evaluating Stress among Family Caregivers of Hemodialysis Patients with End-Stage Renal Disease

Article Record

Md. Rabby[§]
ORCID 0009-0002-8608-8332



Prof. Chinna Chadayan^{§§*}
Professor
ORCID 0000-0001-8793-4671
*Corresponding Author



Prof. D. Melba Sahaya
Sweety^{§§}
Associate Professor
ORCID 0000-0001-7491-804X



§ Enam Nursing College, Enam Medical College and Hospital, Dhaka, Bd (OA)

RECEIVED
2026-03-04

ACCEPTED
2026-03-10

PUBLISHED
2026-04-04

PEER REVIEW
Double Blind

Abstract

Background: Chronic kidney disease (CKD) is a progressive condition leading to end-stage renal disease (ESRD), often requiring hemodialysis. Hemodialysis imposes significant physical and psychological demands not only on patients but also on family members, who serve as primary caregivers. High caregiver stress can adversely affect both caregiver well-being and patient outcomes.

Objectives: This study aimed to assess the level of stress among family members of patients undergoing hemodialysis and to examine its association with socio-demographic and patient-related factors.

Methods: A descriptive cross-sectional design was employed involving 120 family caregivers at a selected hospital in Gazipur, Dhaka. Data were collected using a structured socio-demographic questionnaire and the Kingston Caregiver Stress Scale. Descriptive statistics summarized caregiver characteristics and stress levels, while Chi-square and t-tests assessed associations with selected variables.

Results: Findings revealed that 74.2% of caregivers experienced severe stress, 25% moderate stress, and 0.8% low stress. Stress levels were significantly associated with age, gender, family type, marital status, income, area of residence, and patient condition severity. Younger caregivers, males, those from nuclear families, and caregivers of patients with severe illness reported higher stress.

Conclusion: Family caregivers of hemodialysis patients experience substantial stress influenced by multiple socio-demographic and patient-related factors. Integrating targeted interventions, including counseling, educational programs, and social support, into routine hemodialysis care is essential to reduce stress, enhance caregiver well-being, and improve patient outcomes.

Caregiver stress

Hemodialysis

End-stage renal disease

Family caregivers

Bangladesh

AI USE STATEMENT

No generative AI was used for analysis or results.

FUNDING

This research received no specific grant or funding from any sector.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

DATA AVAILABILITY

Not applicable for this article.

ETHICS

No ethics committee approval was required for this article type.

CONSENT

Not applicable for this article.

TRIAL REG.

Not applicable.

Crossref DOI: 10.34257/GJMRVOL26IS1PG11

How to Cite: Rabby et al. (2026). Evaluating Stress among Family Caregivers of Hemodialysis Patients with End-Stage Renal Disease. Global Journal of Medical Research, 26(1), 7-13. DOI: 10.34257/GJMRVOL26IS1PG11

LICENSE

© 2026 Global Journals. Open-access article under CC BY-NC-ND 4.0 International License.



Print ISSN 0975-5888



Online ISSN 2249-4618



Under the strict compliance and defined process of



METADATA CONTINUATION

AUTHOR CONTACT QR LEDGER

Md.Rabby§ 	Prof. Chinna Chadayan§ð* 	Prof. D.Melba Sahaya Sweety§ξ 
--	---	---

ARCHIVAL RECORD

Evaluating Stress among Family Caregivers of Hemodialysis Patients with End-Stage Renal Disease

Md.Rabby[§] , Prof. Chinna Chadayan^{§§*} , and Prof. D.Melba Sahaya Sweetey^{§§} 

Affiliations

§ Enam Nursing College, Enam Medical College and Hospital, Dhaka, Bd (OA)

Qualifications / Designations

§ Professor

§ Associate Professor

Abstract

Background: Chronic kidney disease (CKD) is a progressive condition leading to end-stage renal disease (ESRD), often requiring hemodialysis. Hemodialysis imposes significant physical and psychological demands not only on patients but also on family members, who serve as primary caregivers. High caregiver stress can adversely affect both caregiver well-being and patient outcomes.

Objectives: This study aimed to assess the level of stress among family members of patients undergoing hemodialysis and to examine its association with socio-demographic and patient-related factors.

Methods: A descriptive cross-sectional design was employed involving 120 family caregivers at a selected hospital in Gazipur, Dhaka. Data were collected using a structured socio-demographic questionnaire and the Kingston Caregiver Stress Scale. Descriptive statistics summarized caregiver characteristics and stress levels, while Chi-square and t-tests assessed associations with selected variables.

Results: Findings revealed that 74.2% of caregivers experienced severe stress, 25% moderate stress, and 0.8% low stress. Stress levels were significantly associated with age, gender, family type, marital status, income, area of residence, and patient condition severity. Younger caregivers, males, those from nuclear families, and caregivers of patients with severe illness reported higher stress.

Conclusion: Family caregivers of hemodialysis patients experience substantial stress influenced by multiple socio-demographic and patient-related factors. Integrating targeted interventions, including counseling, educational programs, and social support, into routine hemodialysis care is essential to reduce stress, enhance caregiver well-being, and improve patient outcomes.

Keywords: Caregiver stress, Hemodialysis, End-stage renal disease, Family caregivers, Bangladesh

* Corresponding Author

Prof. Chinna Chadayan

DOI

10.34257/GJMRFVOL26IS1PG11

1. INTRODUCTION

Chronic kidney disease (CKD) is a progressive, irreversible condition characterized by a gradual decline in kidney function, ultimately leading to end-stage renal failure (ESRD), which requires renal replacement therapies such as hemodialysis (HD) or kidney transplantation for survival (Cao, Chen, Liu, Wu, & Gao, 2025). CKD has emerged as a major global public health challenge, with prevalence rising due to aging populations, lifestyle changes, and increasing rates of diabetes and hypertension (Cao et al., 2025). In Bangladesh, CKD incidence is particularly concerning, with many patients affected by comorbidities and limited access to specialized care (Kar & Islam, 2023; Fatemaa et al., 2025). For most ESRD patients in low- and middle-income countries, hemodialysis remains the most accessible and life-sustaining treatment (Kar & Islam, 2023).

Hemodialysis is the most commonly used treatment for kidney failure. It is a procedure in which a dialysis machine and a special filter—also known as an artificial kidney or dialyzer—are used to remove waste products and excess fluids from the blood when kidney function is impaired. The number of individuals undergo-

ing hemodialysis is increasing each year. This time-intensive and expensive therapy imposes both physical and psychosocial stress, creating a significant burden on patients and their families (George, Zaidi, & Kazmi, 2022). Hemodialysis is often considered a “family illness,” with family caregivers serving as essential partners in the therapeutic process. Caregivers frequently prioritize the needs of patients over their own, spending less time on health-promoting activities, which adversely affects their own health and disrupts their daily routines (Ebadi, Sajadi, Moradian, & et al., 2021).

While life-saving, hemodialysis imposes substantial physical and psychological demands on patients. Common physiological challenges include fatigue, anemia, vascular access complications, and cardiovascular comorbidities (Hejazi, Hosseini, Ebadi, & et al., 2021). Patients must also adhere to strict dietary and fluid restrictions, frequent hospital visits, and lengthy dialysis sessions multiple times per week (George, Zaidi, & Kazmi, 2022). These challenges extend to family members, who act as informal caregivers and bear significant responsibility in ensuring treatment adherence, monitoring complications, and providing emotional and practical support (Ebadi, Sajadi, Moradian, & et al., 2021).

Family caregivers play a pivotal role in ESRD management, yet caregiving is often associated with high levels of stress and reduced quality of life (QoL) (Akbari, Farsi, & Sajadi, 2023; Pio, Prihanto, Jahan, Hirose, Kazawa, & Moriyama, 2022). In South Asia, family caregiving is strongly influenced by cultural expectations, with emotional bonds and familial obligations promoting close involvement in patient care (Khouban-Shargh, Mirhosseini, Ghasempour, & et al., 2024). While this involvement can improve patient outcomes, it frequently leads to psychological and social burdens, including anxiety, depression, and social isolation, adversely affecting both caregiver well-being and the quality of care provided (Akbari et al., 2023; George et al., 2022; Pio et al., 2022).

Caregiver burden encompasses both objective and subjective dimensions. Objective burden refers to tangible disruptions such as time constraints, reduced social interactions, and physical strain, while subjective burden involves emotional and psychological responses, including stress, frustration, and feelings of inadequacy (Ebadi et al., 2021). Evidence indicates that caregiver stress intensifies as patients' disease progresses or as treatment complexity increases, potentially leading to burnout and reduced caregiving capacity (Khouban-Shargh et al., 2024; Al Maqbali, Al Omari, Abu Sharour, & et al., 2025). In Bangladesh, financial challenges, limited access to renal replacement therapy, and inadequate health-care infrastructure exacerbate caregiver stress, creating a unique burden for family members (Fatemaa et al., 2025; Kar & Islam, 2023).

Perceived stress reflects a caregiver's appraisal of their ability to manage caregiving demands. High levels of perceived stress are associated with anxiety, depression, and decreased QoL (Khouban-Shargh et al., 2024; Al Maqbali et al., 2025; George et al., 2022). Stress often has reciprocal effects: as patients experience physical or emotional distress, caregiver stress increases, which can negatively impact patient care and outcomes (Ebadi et al., 2021; Hejazi et al., 2021). Studies in Indonesia and Iran report that family caregivers of hemodialysis patients commonly experience moderate to high levels of stress, highlighting the global relevance of this issue (Pio et al., 2022; Khouban-Shargh et al., 2024).

Stress management and social support are key factors in mitigating caregiver stress. Structured programs that focus on adaptive coping strategies, problem-solving, relaxation techniques, and emotional regulation can significantly reduce perceived stress and enhance QoL and caregiving effectiveness (Khouban-Shargh et al., 2024; Al Maqbali et al., 2025). Social support from family, friends, or community networks reduces perceived stress, improves coping, and strengthens caregivers' ability to provide effective patient care (George et al., 2022; Pio et al., 2022).

Despite growing awareness of caregiver stress, research specifically focusing on family caregivers in low- and middle-income countries, including Bangladesh, remains limited. Local evidence suggests caregivers face unique challenges due to insufficient healthcare resources, financial constraints, and social pressures (Kar & Islam, 2023; Fatemaa et al., 2025). Understanding the prevalence and determinants of stress among caregivers is therefore essential for designing culturally appropriate interventions that enhance both caregiver well-being and patient outcomes.

ESRD and hemodialysis impose considerable psychological and social demands on family caregivers. High levels of stress among caregivers negatively affect QoL and caregiving capacity (Akbari et al., 2023; Khouban-Shargh et al., 2024; George et al., 2022; Pio et al., 2022). Addressing caregiver stress through structured interventions and strong social support networks is crucial for holistic

ESRD management, particularly in resource-limited settings like Bangladesh. This study aims to assess the level of stress among family caregivers of patients undergoing hemodialysis and identify contributing factors to guide interventions that improve caregiver and patient outcomes.

2. MATERIALS AND METHODS

2.1. Research Approach

A quantitative research approach was adopted to systematically examine the stress levels experienced by family members of patients with end-stage renal failure undergoing hemodialysis. This approach facilitated the collection of numerical data that could be statistically analyzed, allowing for objective measurement and reliable conclusions regarding caregivers' stress.

2.2. Research Design

A descriptive cross-sectional design was employed to provide a snapshot of the stress levels and coping mechanisms among family members at a specific point in time. This design enabled the study to explore and describe the experiences and challenges of patients in the hemodialysis unit.

2.3. Sample

The study population comprised family members of patients undergoing hemodialysis at a selected Hospital in Gazipur, Dhaka. The accessible population included family members present during the data collection period who consented to participate. Using a non-probability convenience sampling technique, a total of 120 participants were selected.

2.4. Criteria for Sample Selection

Inclusion Criteria: The study included family members who accompanied patients during hemodialysis and provided essential support. Participants were required to be present during the data collection period and be aged 25 years or older.

Exclusion Criteria: Family members who were not directly related to the patient, such as friends or extended relatives, were excluded. Additionally, those who were unwilling to participate, unable to read or write in Bangla, absent during the data collection period, or younger than 25 years were not considered for the study.

2.5. Tool for Data Collection

Data were collected using a structured questionnaire consisting of two sections. Section A gathered socio-demographic information, including age, gender, education, occupation, relationship to the patient, and other relevant characteristics. Section B employed the Kingston Caregiver Stress Scale (KCSS), a standardized 10-item instrument designed to assess caregiver stress. Each item was rated on a 5-point Likert scale, where 1 indicated "No Stress" and 5 indicated "Extreme Stress." Total scores ranged from 10 to 50 and were categorized as Low Stress (10–20), Moderate Stress (21–30), High Stress (31–40), and Extreme Stress (41–50). The KCSS was validated and culturally adapted into Bangla for use in this study to ensure clarity and appropriateness for participants (Sadak et al., 2017; García-Martínez et al., 2021).

2.6. Data Collection Procedure

After obtaining ethical approval and hospital permission, participants were approached in the waiting area of the hemodialysis unit. The researcher explained the study purpose, obtained informed consent, and provided the structured questionnaire. Participants

completed the self-administered questionnaire in 15–20 minutes, with clarification provided as needed.

2.7. Data Processing and Analysis

Data were coded and analyzed using descriptive statistics (frequency, percentage, mean, standard deviation) for demographic variables. Inferential statistics, specifically the Chi-square test, were employed to assess associations between stress levels and selected socio-demographic variables. Study findings were presented in tables and graphs (bar charts and pie charts).

2.8. Ethical Considerations

The study adhered to the principles of the Declaration of Helsinki and received ethical clearance from the Institutional Ethical Review Board (IERB) of selected institution (Approval No: EMC/IERB/2024/10-17, October 29, 2024). Participants were provided with detailed information sheets and consent forms indicating the purpose, methods, and voluntary nature of the study. The participation was risk-free to the participants, and confidentiality and anonymity were guaranteed at all stages of the study. In addition, institutional clearance was also obtained from the study site prior to data collection.

3. RESULTS

Table 1 reveals that most family members accompanying patients with end-stage renal failure undergoing hemodialysis were aged 20–30 years (31.7%), followed by those aged 41–50 years (27.5%) and 31–40 years (24.2%), with 16.7% aged 51 years and above. Slightly more than half were male (53.3%), and the majority were married (65.8%) and Muslim (81.7%). High school education was most common (31.7%), and housewives formed the largest occupational group (28.3%), followed by private employees (16.7%) and government employees and farmers (12.5% each). Most participants belonged to joint families (59.2%) and were spouses of the patients (45.0%). Family income was fairly distributed, with 31.7% earning above BDT 20,001. Participants predominantly resided in rural areas (42.5%), followed by semi-urban (37.5%) and urban areas (20.0%). The majority were always present with the patient (41.7%), and most patients' conditions were of moderate severity (60.0%).

Table 2 reveals that the majority of family members of patients with end-stage renal failure undergoing hemodialysis experienced severe stress, accounting for 74.2% of the sample. A smaller proportion reported moderate stress (25.0%), while only 0.8% of participants experienced low stress. This indicates that most family members face a high level of psychological burden while caring for patients undergoing hemodialysis.

Table 3 reveals that stress levels among family members of patients undergoing hemodialysis were significantly associated with age, gender, and occupation. Severe stress was most prevalent across all age groups, particularly among participants aged 31–40 years (24.2%) and 20–30 years (22.5%). Gender differences were also evident, with a higher proportion of males (45.8%) experiencing severe stress compared to females (28.3%), while moderate stress was slightly higher among females (17.5%) than males (7.5%). Occupation showed a significant association with stress, with severe stress being more common among private employees (14.2%) and government employees (5.8%), whereas moderate stress was observed mainly among government employees (6.7%). These findings indicate that age, gender, and occupation are important

factors influencing the psychological burden of family members caring for patients undergoing hemodialysis.

Table 4 reveals that mean stress scores among family members of patients undergoing hemodialysis differed significantly across several selected variables. Age was significantly associated with stress ($F = 9.69, p < 0.01$), with the highest mean stress observed in the 31–40 years group (36.89 ± 3.00) and the lowest in those aged 51+ years (30.55 ± 3.73). Gender also showed a significant difference ($t = 2.51, p = 0.01$), with males (34.60 ± 5.45) having slightly higher stress than females (34.44 ± 3.00). Family type influenced stress levels significantly ($t = 5.46, p < 0.01$), with participants from nuclear families (36.12 ± 3.58) experiencing higher stress than those from joint families (31.85 ± 4.58).

Table 1. Distribution of Demographic Variables among Family Members (N = 120)

Demographic Variable	Category	n	%
Age (years)	20–30	38	31.7
	31–40	29	24.2
	41–50	33	27.5
	51 and above	20	16.7
Gender	Male	64	53.3
	Female	56	46.7
Marital Status	Unmarried	38	31.7
	Married	79	65.8
	Others	3	2.5
Religion	Islam	98	81.7
	Hindu	17	14.2
	Christian	4	3.3
	Buddhist	1	0.8
Level of Education	No formal education	19	15.8
	Primary school	30	25.0
	High school	38	31.7
	Collegiate	33	27.5
Occupation	Government employee	15	12.5
	Private employee	20	16.7
	Retired	9	7.5
	Farmer	15	12.5
	Daily worker	8	6.7
	Student	12	10.0
	Businessperson	7	5.8
	Housewife	34	28.3

Table 2. Distribution of Stress Levels among Family Members (N = 120)

Level of Stress	n	%
Low	1	0.8
Moderate	30	25.0
Severe	89	74.2

Table 3. Association between Stress Levels and Socio-Demographic Variables

Demographic Variable	Low Stress n (%)	Moderate Stress n (%)	Severe Stress n (%)	χ^2	p-value
Age (years)				19.1	<0.01
20–30	1 (0.8)	10 (8.3)	27 (22.5)		
31–40	0	0	29 (24.2)		
41–50	0	10 (8.3)	23 (19.2)		
51+	0	10 (8.3)	10 (8.3)		
Gender				10.79	<0.01
Male	0	9 (7.5)	55 (45.8)		
Female	1 (0.8)	21 (17.5)	34 (28.3)		
Occupation				24.41	0.04
Govt. Employee	0	8 (6.7)	7 (5.8)		
Private Employee	1 (0.8)	2 (1.7)	17 (14.2)		
Others	—	—	—		

Table 4. Comparison of Stress Levels by Selected Variables

Variable	Category	Mean Stress Score	SD	df	F/t	p-value	CI
Age	20–30	33.36	5.45	3	9.69	<0.01	—
	31–40	36.89	3.00				
	41–50	32.81	3.82				
	51+	30.55	3.73				
Gender	Male	34.60	5.45	—	2.51	0.01	0.45–3.87
	Female	34.44	3.00				
Family Type	Nuclear	36.12	3.58	—	5.46	<0.01	2.71–5.80
	Joint	31.85	4.58				
Marital Status	Married	32.73	4.54	2	6.55	<0.01	—
	Unmarried	35.68	4.44				
	Others	30.00	1.73				
Monthly Income	5001–10000	34.28	4.09	3	5.23	<0.01	—
	10001–15000	36.21	3.45				
	15001–20000	31.51	5.77				
	Above 20001	33.32	3.97				
Area of Residence	Rural	32.66	4.82	2	5.66	<0.01	—
	Semi-Urban	35.37	4.31				
	Urban	32.25	4.15				
Patient Condition	Mild	31.72	6.33	2	13.59	<0.01	—
	Moderate	32.62	3.95				
	Severe	37.06	3.35				

4. DISCUSSION

The findings of this study provide a comprehensive understanding of the demographic characteristics, stress levels, and associated factors among family caregivers of patients undergoing hemodialysis. As shown in Table 1, the majority of caregivers were young adults aged 20–30 years (31.7%), followed by those aged 41–50 years (27.5%) and 31–40 years (24.2%). This predominance of younger caregivers aligns with international evidence indicating that adult children and spouses commonly assume caregiving responsibilities, particularly in contexts where institutional support for chronic illness is limited (Ebadi et al., 2021; Al Maqbali et al., 2025). The slightly higher proportion of male caregivers (53.3%) contrasts with studies reporting a predominance of female caregivers (Tudayan-Espiritu, 2024; Shukri et al., 2020), suggesting context-specific socio-cultural dynamics may influence caregiving roles, such as male participation in hospital accompaniment and family decision-making. Most participants were married (65.8%) and identified as spouses of the patients (45.0%), emphasizing the central role of familial relationships in caregiving and supporting Tao et al.'s (2023) dyadic framework, which recognizes the interdependent health outcomes of patients and their caregivers.

Educational attainment and occupational status emerged as key factors influencing caregiver stress. High school education was most common (31.7%), while housewives constituted the largest occupational group (28.3%), followed by private (16.7%) and government employees (12.5%). Prior studies have indicated that lower educational attainment may limit health literacy and coping strategies, thereby exacerbating stress (Padekar et al., 2024; Surani et al., 2021). However, the observed stress among employed caregivers highlights the additional burden imposed by work responsibilities, supporting the assertion that professional demands interact with caregiving duties to heighten psychological strain (Intas et al., 2020). Furthermore, most participants lived in joint family systems (59.2%) and rural areas (42.5%), factors previously identified as moderating stress through enhanced social support and shared caregiving responsibilities (Tao et al., 2023; Sułkowski et al., 2024).

Table 2 demonstrates that an overwhelming 74.2% of caregivers experienced severe stress, with only 0.8% reporting low stress. These findings are consistent with existing literature showing high prevalence of psychological distress—including anxiety, depression, and sleep disturbances—among caregivers of hemodialysis patients (Gerogianni et al., 2021; Shukri et al., 2020; Intas et al., 2020). The severity of stress reflects the complex and enduring nature of caregiving, which often requires managing patients' medical needs, emotional support, and coordination with health-care systems, potentially leading to significant psychosocial strain (Ebadi et al., 2021).

The associations between stress and caregiver characteristics (Tables 3 and 4) further elucidate the determinants of psychological burden. Younger caregivers, particularly those aged 20–40 years, reported the highest stress levels, possibly due to competing personal, occupational, and familial responsibilities (Al Maqbali et al., 2025). Gender differences were also notable, with males exhibiting slightly higher mean stress scores than females. This finding diverges from prior studies emphasizing higher female stress, suggesting that contextual factors—such as economic responsibilities, primary decision-making roles, or the nature of patient accompaniment—may amplify stress among male caregivers in this setting (Tudayan-Espiritu, 2024).

Occupational status and income were significantly associated with stress levels, with caregivers in the 10,001–15,000 BDT range experiencing the highest stress. This underscores the role of financial strain in exacerbating caregiver burden, in line with prior evidence linking economic hardship to psychological distress (Al Maqbali et al., 2025; Padekar et al., 2024). Additionally, semi-urban residents reported higher stress levels, possibly reflecting the challenges of limited healthcare infrastructure, travel requirements for treatment, and competing work obligations. Family structure also influenced stress: participants from nuclear families experienced higher stress than those from joint families, highlighting the buffering role of extended family support in mitigating caregiver burden (Tao et al., 2023; Surani et al., 2021).

Crucially, patient-related factors, particularly the severity of illness, were strongly associated with caregiver stress. Caregivers attending to patients in severe condition reported the highest stress levels (37.06 ± 3.35), indicating that caregiving demands escalate as patient health deteriorates. This finding corroborates the dyadic illness management theory, which emphasizes the interconnectedness of patient and caregiver well-being (Tao et al., 2023). It also suggests that interventions must consider both patient clinical status and caregiver psychosocial needs to effectively reduce stress and improve overall outcomes.

While these results are broadly consistent with the literature, several critical considerations warrant attention. First, the predominance of severe stress among caregivers may reflect the study's hospital-based sampling, which could overrepresent caregivers of more critically ill patients. Second, the reliance on self-reported measures may introduce response bias, potentially inflating perceived stress levels. Third, socio-cultural and economic contexts may limit the generalizability of findings to other populations or healthcare settings. Despite these limitations, the study provides valuable insights into the factors influencing caregiver stress and highlights the urgent need for targeted interventions.

Practical implications are clear. Structured family-based interventions, including educational programs, counseling, respite services, and financial guidance, have demonstrated effectiveness in reducing caregiver burden and improving quality of life (Surani et al., 2021; Intas et al., 2020). Moreover, early identification of high-risk caregivers based on demographic and patient-related factors—such as age, family type, income, and patient illness severity—can enable proactive psychosocial support. Policy initiatives should integrate caregiver support into routine hemodialysis care, including stress management programs, social support enhancement, and training to improve coping strategies. Such interventions may not only enhance caregiver well-being but also indirectly improve patient adherence and clinical outcomes.

5. CONCLUSION

Caregivers of hemodialysis patients experience substantial psychological burden, with stress levels influenced by demographic, socio-economic, familial, and patient-related factors. Younger caregivers, males, those from nuclear families, and individuals with lower income or caring for patients in severe conditions are particularly vulnerable to elevated stress. These findings highlight the urgent need for support strategies that address both the practical and emotional challenges of caregiving. Interventions such as counseling, educational programs, respite services, and enhanced social support can reduce stress, improve quality of life, and promote more effective caregiving. Integrating caregiver-focused initiatives into routine hemodialysis care is essential not

only to safeguard caregiver well-being but also to improve patient outcomes, ensuring a holistic and sustainable approach to chronic kidney disease management.

■ REFERENCES

- [1] Akbari, R., Farsi, Z., & Sajadi, S. A. (2023). Relationship between fatigue and quality of life and related factors in family caregivers of patients on hemodialysis. *BMC Psychiatry*, 23, 430. <https://doi.org/10.1186/s12888-023-04934-2>
- [2] Al Maqbali, A., Al Omari, O., Abu Sharour, L., & et al. (2025). The perceived levels of stress, anxiety, and depression among family caregivers of patients undergoing haemodialysis and their association with quality of life. *BJPsych Open*, 11(3), e100. <https://doi.org/10.1192/bjo.2025.44>
- [3] Cao, Y., Chen, H., Liu, H., Wu, H., & Gao, W. (2025). Global, regional, and national temporal trends in incidence for type 2 diabetes mellitus-related chronic kidney disease from 1992 to 2021. *Diabetes & Metabolism Journal*, 49(4), 848–861. <https://doi.org/10.4093/dmj.2024.0593>
- [4] Ebadi, A., Sajadi, S. A., Moradian, S. T., & et al. (2021). Psychological consequences for family caregivers of patients receiving hemodialysis: Threat or opportunity? *BMC Psychology*, 9, 154. <https://doi.org/10.1186/s40359-021-00667-7>
- [5] Fatemaa, K., Khatunb, A. A., Aktar Brisrtya, S., Islamc, M. A., Kabirc, F. N. A., Nayanc, S. B., Afrinc, A., Sathidand, T. R., & Halimc, M. A. (2025). Analytical studies on chronic kidney disease and associated lifestyle risk factors among the patients of different hospitals in Dhaka City, Bangladesh. *Asian Journal of Research in Nephrology*, 8(1), 1–15. <https://doi.org/10.9734/ajrn/2025/v8i187>
- [6] García-Martínez, M., López-Gómez, J., & Rodríguez-Pérez, J. (2021). Perceived stress in relation to quality of life and resilience in patients with advanced chronic kidney disease undergoing hemodialysis. *International Journal of Environmental Research and Public Health*, 18(2), 536. <https://doi.org/10.3390/ijerph18020536>
- [7] George, S., Zaidi, S. Z. H., & Kazmi, S. S. H. (2022). Stress, anxiety, and perceived social support among hemodialysis patients with chronic kidney disease. *International Journal of Health Sciences*, 6(S1), 9494–9507. <https://doi.org/10.53730/ijhs.v6nS1.7184>
- [8] Gerogianni, G., et al. (2021). Factors affecting anxiety and depression in caregivers of hemodialysis patients. In P. Vlamos (Ed.), *GeNeDis 2020. Advances in Experimental Medicine and Biology* (Vol. 1337, pp. 59–70). Springer. https://doi.org/10.1007/978-3-030-78771-4_6
- [9] Hejazi, S. S., Hosseini, M., Ebadi, A., & et al. (2021). Components of quality of life in hemodialysis patients from family caregivers' perspective: A qualitative study. *BMC Nephrology*, 22, 379. <https://doi.org/10.1186/s12882-021-02584-8>
- [10] Intas, G., Rokana, V., Stergiannis, P., Chalari, E., & Anagnostopoulos, F. (2020). Burden and sleeping disorders of family caregivers of hemodialysis patients with chronic kidney disease-end stage: A cross-sectional study. In P. Vlamos (Ed.), *GeNeDis 2018. Advances in Experimental Medicine and Biology* (Vol. 1196, pp. 41–51). Springer. https://doi.org/10.1007/978-3-030-32637-1_4
- [11] Kar, S., & Islam, M. F. (2023). Global dialysis perspective: Bangladesh. *Kidney360*, 4(10), e1472–e1475. <https://doi.org/10.34067/KID.0000000000000232>
- [12] Khouban-Shargh, R., Mirhosseini, S., Ghasempour, S., & et al. (2024). Stress management training program to address caregiver burden and perceived stress among family caregivers of patients undergoing hemodialysis: A randomized controlled trial study. *BMC Nephrology*, 25, 350. <https://doi.org/10.1186/s12882-024-03795-5>
- [13] Padekar, M. R., et al. (2024). Assess the quality of life of caregivers of patients undergoing hemodialysis among selected hospitals. *Educational Administration: Theory and Practice*, 30(11), 1466–1474. <https://doi.org/10.53555/kuey.v30i11.9518>
- [14] Pio, T. M. T., Prihanto, J. B., Jahan, Y., Hirose, N., Kazawa, K., & Moriyama, M. (2022). Assessing Burden, Anxiety, Depression, and Quality of Life among Caregivers of Hemodialysis Patients in Indonesia: A Cross-Sectional Study. *International Journal of Environmental Research and Public Health*, 19(8), 4544. <https://doi.org/10.3390/ijerph19084544>
- [15] Sadak, T., Korpak, A., Wright, J. D., Lee, M. K., Noel, M., Buckwalter, K., & Borson, S. (2017). Psychometric evaluation of Kingston Caregiver Stress Scale. *Clinical Gerontologist*, 40(4), 268–280. <https://doi.org/10.1080/07317115.2017.1313349>
- [16] Shukri, M., Mustofai, M. A., Md Yasin, M. A. S., & Tuan Hadi, T. S. (2020). Burden, quality of life, anxiety, and depressive symptoms among caregivers of hemodialysis patients: The role of social support. *The International Journal of Psychiatry in Medicine*, 55(6), 397–407. <https://doi.org/10.1177/0091217420913388>
- [17] Sułkowski, L., Matyja, A., & Matyja, M. (2024). Social support and quality of life in hemodialysis patients: A comparative study with healthy controls. *Medicina*, 60(11), 1732. <https://doi.org/10.3390/medicina60111732>
- [18] Surani, V., Suza, D. E., & Tarigan, M. (2021). The impact of family intervention programs on the caregiver burden of hemodialysis patients. *KONTAKT-Journal of Nursing and Social Sciences Related to Health and Illness*, 23(2), 138–145. <https://doi.org/10.32725/kont.2021.017>
- [19] Tao, Y., Liu, T., Zhuang, K., Fan, L., Hua, Y., & Ni, C. (2023). Perceived stress, social support, and insomnia in hemodialysis patients and their family caregivers: An actor-partner interdependence mediation model analysis. *Frontiers in Psychology*, 14, 1172350. <https://doi.org/10.3389/fpsyg.2023.1172350>
- [20] Tudayan-Espiritu, C. (2024). Stress, appraisal, coping, and adaptation of family caregivers of patients on dialysis: A transactional theory approach. *Journal of Interdisciplinary Perspectives*, 2(5), 161–166. <https://doi.org/10.69569/jip.2024.0073>



Conceptual and Biological Inconsistencies in the Insulin Resistance Paradigm of Type 2 Diabetes

Article Record

Dr. John M Poothullil MD, FRCP*
*Corresponding Author



RECEIVED
2026-03-12

ACCEPTED
2026-03-21

PUBLISHED
2026-04-04

PEER REVIEW
Double Blind

Abstract

Type 2 diabetes mellitus (T2DM) is commonly attributed to insulin resistance, defined as impaired responsiveness of skeletal muscle, adipose tissue, and liver to insulin. Although the concept is deeply embedded in modern metabolic medicine, it remains largely inferential and descriptive. This paper critically examines the conceptual, physiological, and epidemiological limitations of the insulin resistance paradigm. It argues that the model lacks a demonstrated unifying mechanism capable of coordinating selective impairment across multiple tissues, does not adequately explain preservation of many insulin-mediated functions, and leaves unresolved several clinical paradoxes, including rapid reversibility of hyperglycemia, metabolically healthy obesity, and diabetes in lean individuals. The paper further argues that the speed with which T2DM prevalence has risen is difficult to reconcile with explanations grounded in intrinsic cellular defects or evolutionary adaptation. An alternative interpretation based on chronic substrate overload and altered metabolic flux is presented as a more coherent framework for understanding the observed phenotype. This reinterpretation has implications for both research priorities and therapeutic strategy, suggesting that reduction of metabolic load and restoration of substrate balance may be central to effective management. Reassessment of insulin resistance as a primary causal construct may therefore be necessary for progress in the prevention and treatment of type 2 diabetes.

Type 2 diabetes

Insulin resistance

Hyperglycemia

Substrate overload

Metabolic flux

Nutrient excess

Ectopic fat

AI USE STATEMENT

No generative AI was used for analysis or results.

FUNDING

No external funding was declared for this work.

CONFLICT OF INTEREST

I have published several consumer books about Type 2 diabetes based on my hypothesis that dietary change can prevent or...

DATA AVAILABILITY

Not applicable for this article.

ETHICS

No ethics committee approval was required for this article type.

CONSENT

Not applicable for this article.

TRIAL REG.

Not applicable.

Crossref DOI: 10.34257/GJMRF256048

How to Cite: Poothullil MD, FRCP (2026). Conceptual and Biological Inconsistencies in the Insulin Resistance Paradigm of Type 2 Diabetes. Global Journal of Medical Research, 26(1), 14-18. DOI: 10.34257/GJMRF256048

LICENSE

© 2026 Global Journals. Open-access article under CC BY-NC-ND 4.0 International License.



Print ISSN 0975-5888



Online ISSN 2249-4618



Under the strict compliance and defined process of



METADATA CONTINUATION

AUTHOR CONTACT QR LEDGER

Dr. John M Poothullil MD,
FRCP*



ARCHIVAL RECORD

Conceptual and Biological Inconsistencies in the Insulin Resistance Paradigm of Type 2 Diabetes

Dr. John M Poothullil MD, FRCP*

Abstract

Type 2 diabetes mellitus (T2DM) is commonly attributed to insulin resistance, defined as impaired responsiveness of skeletal muscle, adipose tissue, and liver to insulin. Although the concept is deeply embedded in modern metabolic medicine, it remains largely inferential and descriptive. This paper critically examines the conceptual, physiological, and epidemiological limitations of the insulin resistance paradigm. It argues that the model lacks a demonstrated unifying mechanism capable of coordinating selective impairment across multiple tissues, does not adequately explain preservation of many insulin-mediated functions, and leaves unresolved several clinical paradoxes, including rapid reversibility of hyperglycemia, metabolically healthy obesity, and diabetes in lean individuals. The paper further argues that the speed with which T2DM prevalence has risen is difficult to reconcile with explanations grounded in intrinsic cellular defects or evolutionary adaptation. An alternative interpretation based on chronic substrate overload and altered metabolic flux is presented as a more coherent framework for understanding the observed phenotype. This reinterpretation has implications for both research priorities and therapeutic strategy, suggesting that reduction of metabolic load and restoration of substrate balance may be central to effective management. Reassessment of insulin resistance as a primary causal construct may therefore be necessary for progress in the prevention and treatment of type 2 diabetes.

Keywords: Type 2 diabetes, Insulin resistance, Hyperglycemia, Substrate overload, Metabolic flux, Nutrient excess, Ectopic fat, Pathophysiology

* Corresponding Author
Dr. John M Poothullil MD, FRCP

DOI
10.34257/GJMRF256048

1. Introduction

Type 2 diabetes mellitus has become one of the most consequential chronic diseases of modern medicine. Its prevalence has risen sharply within a historically brief period, both in the United States and globally. Earlier national estimates placed diabetes at a comparatively low prevalence in the mid-twentieth century, whereas current estimates show a many-fold increase, now affecting a large share of adults. The scale and speed of this rise demand a careful re-examination of the dominant causal framework used to explain hyperglycemia in T2DM [1, 2].

The prevailing model holds that T2DM develops because skeletal muscle, adipose tissue, and liver become resistant to insulin. In this account, muscle fails to take up glucose efficiently, adipose tissue does not adequately suppress lipolysis, and the liver continues to release glucose despite circulating insulin. Hyperinsulinemia is then interpreted as a compensatory response to diminished insulin action. This framework has shaped research priorities, clinical language, drug development, and public understanding of diabetes for decades [3].

Yet the apparent explanatory success of the insulin resistance model has masked a series of unresolved problems. The term itself often functions more as an interpretation of measured glucose dynamics than as a directly demonstrated lesion in cell biology. Measures such as HOMA-IR and clamp studies quantify relationships among glucose uptake, glucose production, and insulin concentration, but they do not directly identify a primary molecular defect that causes those relationships. In effect, the field observes altered glucose handling and names the observation

insulin resistance, then uses that label to explain the same observation. The result is a concept with substantial descriptive utility but uncertain causal precision [4, 5].

This paper does not deny that reduced glucose disposal can be observed in T2DM. Rather, it questions whether such observations justify the conclusion that a primary defect in insulin signaling is the central biological driver of the disease. Drawing from prior analyses of conceptual gaps, physiological paradoxes, epidemiological trends, and a set of technical questions regarding substrate competition, this article argues that the insulin resistance paradigm is internally inconsistent in important respects and may not provide the most coherent account of hyperglycemia.

2. Historical Development of the Insulin Resistance Concept

The intellectual history of insulin resistance helps explain why the idea achieved such centrality despite its unresolved ambiguities. Once insulin had been identified as essential for glucose regulation, and once insulin therapy transformed the outlook for patients with Type 1 diabetes, it was natural for clinicians to interpret hyperglycemia broadly through an insulin-centered lens. When adults with diabetes were found to have normal or elevated insulin levels, reduced responsiveness of target tissues appeared to offer a convenient explanation. The concept of insulin resistance thus emerged not from direct observation of a specific molecular failure, but from the need to reconcile hyperglycemia with the presence of insulin [6].

As the twentieth century progressed, this interpretation hardened into doctrine. Classification systems distinguished juvenile from adult-onset diabetes, and the latter became increasingly framed as a disorder of impaired insulin action rather than absolute insulin deficiency. The glucose clamp technique later gave investigators a rigorous way to compare insulin levels with glucose disposal, and lower-than-expected disposal rates were interpreted as evidence that tissues had become resistant. This was an important methodological advance, but it still did not establish why glucose uptake was reduced. It quantified the phenomenon; it did not settle the cause [5].

Over time, the language of insulin resistance acquired a status beyond that warranted by the evidence supporting it. What began as an interpretive construct increasingly came to be treated as a primary lesion that could unify the metabolic abnormalities of T2DM. Yet the historical path by which the concept arose suggests caution. It was inferred from outcomes, generalized across tissues, and then institutionalized in textbooks and treatment paradigms before a unifying biological mechanism had been demonstrated. This history does not invalidate the concept, but it does mean that its causal authority should remain open to scrutiny [5, 6].

3. Definitional and Conceptual Problems

A central weakness of the insulin resistance paradigm lies in its imprecision. In common usage, insulin resistance can refer to reduced whole-body glucose disposal, impaired insulin-stimulated glucose transport, failure of insulin to suppress hepatic glucose production, or a broad syndrome inferred from surrogate indices. These are related but not identical phenomena. Because the term spans multiple levels of description, it can create an illusion of explanatory unity where none has been established [3, 4].

The problem is especially evident in causal reasoning. If elevated glucose and elevated insulin coexist, the relationship is commonly interpreted as evidence that tissues are not responding appropriately to insulin. However, this conclusion is not the only possible interpretation. Hyperglycemia resulting from reduced glucose utilization can arise from changes in substrate availability, intracellular fuel prioritization, storage capacity, hepatic overflow physiology, or adaptive endocrine responses. By treating all such possibilities as instances of insulin resistance, the paradigm risks collapsing distinct mechanisms into a single label [7].

The concept also suffers from circularity. Hyperglycemia leads to tests showing reduced glucose disposal relative to insulin; this pattern is labeled insulin resistance; insulin resistance is then invoked as the cause of hyperglycemia. Unless the underlying lesion is independently demonstrated, the explanation remains tautological. A descriptive index is effectively substituted for a mechanism. This is not a minor semantic concern. In medicine, labels shape therapeutic priorities, and if the causal model is misidentified, treatment strategies may be directed toward downstream manifestations rather than the primary physiological disturbance [4, 5].

From a conceptual standpoint, hyperglycemia may be viewed in a manner analogous to hypercholesterolemia, in that both are defined by elevated circulating biomarkers that may arise from multiple underlying causes. In the case of hypercholesterolemia, elevated lipid levels may reflect dietary factors, genetic conditions, or other metabolic disturbances, rather than a single unifying mechanism. Similarly, hyperglycemia may represent the net effect of diverse physiological processes, including altered substrate availability, storage limitations, and hormonal regulation. Such

an approach has clear clinical utility but also underscores the importance of distinguishing descriptive constructs from primary biological mechanisms.

4. Major Biological Inconsistencies in the Paradigm

In addition to definitional and conceptual problems, several specific biological inconsistencies further challenge the internal coherence of the insulin resistance paradigm.

4.1. No unifying coordinating mechanism across tissues

The standard account requires that skeletal muscle, adipose tissue, and liver all develop some form of diminished insulin responsiveness. Yet these tissues are biologically distinct. They differ in transporter systems, intracellular signaling architecture, fuel priorities, and physiological roles. Despite decades of research, no established signal has been shown to orchestrate a coordinated, selective reduction in insulin responsiveness across all three tissues in a way that explains the core phenotype of T2DM [8].

This absence matters because the paradigm is not merely stating that abnormalities are present in several tissues; it is asserting a common causal process. If billions of cells across different organs are all said to become resistant, the burden is to identify a mechanism capable of inducing and reversing that state. Without such a mechanism, insulin resistance remains a descriptor attached to outcomes rather than a demonstrated biological program [8].

4.2. Selective preservation of other insulin functions

A further inconsistency is the selective nature of the supposed defect. In T2DM, glucose handling is said to be impaired, yet many other insulin-mediated actions remain operative. Protein synthesis continues. Lipogenic and other anabolic processes are not uniformly absent. Basic physiological functions such as maintenance of muscle tone and thermoregulation are preserved. If the primary defect were a generalized failure of insulin signaling, a broader collapse of insulin-mediated actions might be expected. Instead, the picture is one of selective disturbance, concentrated around glucose handling [9].

This selective preservation raises a critical question: why should insulin signaling fail specifically in ways that elevate blood glucose while remaining sufficiently functional for numerous other tasks? The paradigm offers descriptions of pathway complexity, but that is not the same as a unifying explanation. The more selective the impairment, the stronger the need to consider whether cells are reprioritizing fuel use under altered metabolic conditions rather than suffering a primary signaling defect [9].

4.3. Selective vulnerability of insulin versus other hormones

Insulin does not operate in isolation. Glucagon, catecholamines, cortisol, growth hormone, incretins, adipokines, and other signals all influence nutrient handling. Yet the dominant model posits a pathological resistance focused primarily on insulin. Other hormones in the same organism, acting on the same tissues and within the same inflammatory or nutrient milieu, are not typically described as becoming broadly ineffective in parallel. Glucagon continues to stimulate hepatic glucose production. Catecholamines retain lipolytic and cardiovascular effects. Cortisol and growth hormones continue to exert major physiological actions [10].

Table 1. Key Inconsistencies and Contradictions in the Insulin Resistance Paradigm

Inconsistency	Description	Implication
No unifying mechanism	No identified biological signal explains coordinated insulin resistance across muscle, liver, and adipose tissue	Suggests insulin resistance may be descriptive rather than causal
Selective insulin impairment	Glucose metabolism appears impaired while other insulin-mediated functions remain largely intact	Inconsistent with a global signaling defect
Hormonal selectivity	Other hormonal systems (e.g., glucagon, cortisol) remain functional under the same conditions	Challenges the concept of generalized endocrine resistance
Transporter differences	GLUT4 (muscle) and GLUT2 (liver) operate through distinct mechanisms	Complicates the notion of a uniform resistance mechanism
Rapid reversibility	Hyperglycemia improves quickly with caloric restriction	Suggests a dynamic metabolic process rather than fixed cellular defect
Obesity without diabetes	Many individuals with obesity remain metabolically normal	Indicates obesity alone is insufficient to cause T2D
Lean diabetes	Type 2 diabetes occurs in non-obese individuals	Points to factors beyond adiposity
Adipose storage variability	Differences in fat storage capacity influence metabolic outcomes	Supports the concept of a personal fat threshold
Measurement limitations	Insulin resistance is inferred from indirect indices (e.g., HOMA-IR)	Limits causal interpretation

If glucotoxicity, inflammation, or lipotoxicity were sufficient to generate a generalized state of hormonal resistance, a broader endocrine dysfunction might be expected. The selective targeting of insulin is therefore conceptually odd. Why would insulin alone be uniquely vulnerable while neighboring hormonal systems remain substantially intact? This asymmetry weakens the idea that T2DM is fundamentally a hormone resistance disorder and instead suggests that the apparent defect may reflect context-specific limitations on glucose utilization.

4.4. Transporter and tissue inconsistencies

The concept of insulin resistance is often spoken of as though it were uniform across tissues, yet the relevant transport biology differs markedly. Skeletal muscle glucose uptake is linked strongly to GLUT4, whereas hepatic glucose transport is mediated primarily by GLUT2, which is bidirectional and not directly governed by insulin in the same manner. Cardiac muscle also uses GLUT4 yet is not usually discussed in the same simple way as “insulin resistant” skeletal muscle. These discrepancies complicate the idea of a single receptor-level defect producing the same functional syndrome everywhere [11].

In the liver, for example, continued glucose release in the presence of insulin is often called hepatic insulin resistance. But because glucose transport there is structurally different, the mechanism cannot simply be the same as in muscle. Likewise, adipose tissue behavior reflects both storage capacity and ongoing lipolytic signaling, which again differs from muscle physiology. To gather these diverse phenomena under a single heading may be rhetorically convenient, but it risks mechanistic confusion [11].

These inconsistencies, summarized in Table 1, collectively challenge the internal coherence of the insulin resistance paradigm.

5. Clinical and Epidemiological Contradictions

Several clinical and epidemiological observations further challenge the explanatory adequacy of the insulin resistance paradigm.

5.1. Rapid reversibility of hyperglycemia

One of the most difficult observations for the insulin resistance model is the speed with which hyperglycemia can improve. Hypocaloric or very-low-calorie interventions can normalize fasting glucose and reduce hepatic glucose output within days to weeks, often before major changes in peripheral insulin sensitivity are evident. Such rapid improvement is easier to understand if the core disturbance is one of substrate overload, hepatic fat burden, or altered metabolic flux, all of which can change quickly when nutrient intake falls. It is harder to explain if the disease is driven primarily by a stable intrinsic defect in insulin signaling [12, 13].

This does not prove that signaling plays no role, but it suggests that at least some central drivers of hyperglycemia are dynamic, reversible, and closely linked to nutrient conditions. The clinical time course therefore argues against treating insulin resistance as the primary lesion [12, 13].

5.2. Obesity without diabetes and diabetes without obesity

Obesity undoubtedly correlates with diabetes risk, yet correlation is not sufficiency. A substantial fraction of individuals with obesity remain normoglycemic, while a meaningful subset of patients with T2DM are not obese by conventional BMI criteria. Prior material highlighted both metabolically healthy obesity and the increasing prevalence of diabetes in lean individuals, including populations with lower BMI thresholds and different body composition profiles [14, 15].

These findings challenge any simple model in which excess body mass directly causes insulin resistance, which in turn causes T2DM. They are more compatible with variation in fat storage capacity, ectopic fat handling, and substrate overflow. Under such a view, obesity is a risk marker but not the decisive causal variable. What matters is whether incoming nutrient load exceeds the individual's capacity to store, oxidize, or buffer it without disturbing glucose homeostasis [14, 15].

5.3. Diabetes with no intake of excess food, termed malnutrition-associated diabetes

Malnutrition in the womb and early childhood may limit the development of adipose tissue, reducing the number of fat cells available for lipid storage in adulthood. When energy intake later increases, this reduced storage capacity may be exceeded more rapidly, leading to earlier diversion of lipid substrates into the circulation and ectopic tissues. This concept, often described as limited adipose expandability or a “personal fat threshold,” provides a potential explanation for the development of type 2 diabetes in individuals who are not overtly obese [16]. Once this storage capacity is approached or exceeded, increased fatty acid availability may promote substrate competition in muscle and liver, contributing to reduced glucose utilization despite preserved insulin signaling.

5.4. Evolutionary implausibility of the epidemic

The modern diabetes epidemic has unfolded over decades, not millennia. That temporal fact alone creates difficulty for explanations centered on the emergence of intrinsic cellular defects or a widespread biological tendency for humans to become insulin resistant. Prior text correctly emphasized that the dramatic rise in T2DM cannot plausibly reflect recent genetic evolution. Environmental and behavioral changes have occurred far too quickly relative to the pace of genome-wide adaptation [2, 17].

This point is more than rhetorical. If the disease has surged because of rapid changes in food environment, food processing, caloric density, and sustained nutrient excess, then the primary explanatory burden should fall on metabolic conditions created by that environment. A framework that begins with nutrient overload is therefore more historically and epidemiologically plausible than one that begins with spontaneous widespread hormone resistance [17].

6. Alternative Interpretation: Substrate Overload and Altered Metabolic Flux

A more coherent interpretation is that many features of T2DM arise from chronic substrate overload rather than a primary defect in insulin signaling. This framework does not deny that reduced glucose uptake can be measured. It argues instead that the reduction may reflect fuel competition, storage saturation, and overflow physiology. When fatty acids and their metabolites are abundant, tissues may preferentially oxidize fat, thereby suppressing glucose uptake and oxidation without requiring a defect in insulin receptors or downstream signaling pathways. A more detailed formulation of this substrate-based interpretation has been presented elsewhere [18].

Within this view, hepatic glucose overproduction under hyperinsulinemic conditions can be understood as a consequence of substrate handling and storage constraints rather than failed insulin signaling alone. The liver may increase glucose export when glycogen storage is saturated, lipogenic burden is high, and gluconeogenic substrates remain abundant. Because GLUT2 mediates bidirectional glucose equilibration, continued hepatic glucose release need not imply that insulin signaling has collapsed; it may instead reflect overflow metabolism [11, 19].

Fasting hyperglycemia can likewise be interpreted as a flux problem. Persistent fatty acid availability promotes gluconeogenesis and reduces glucose oxidation. Hyperinsulinemia becomes understandable as a physiological response to nutrient excess, attempting to drive storage and maintain glycemic control in an

overloaded system. In this framework, what is commonly called compensatory hyperinsulinemia is not proof of a primary signaling defect but evidence that the organism is dealing with persistent substrate surplus [18, 20].

The same reinterpretation extends to beta-cell behavior. Relative reductions in insulin secretion may represent adaptive limitation rather than primary exhaustion, especially if prolonged hyperinsulinemia itself is metabolically costly. It also clarifies why therapies labeled insulin sensitizing may work even if they do not literally repair a molecular signaling lesion. If treatment reduces hepatic glucose output, lowers caloric intake, decreases ectopic lipid burden, or alters substrate availability, clinical benefit can follow without requiring restoration of a hypothetical primary defect in insulin action [20].

This alternative interpretation also makes sense of pharmacologic treatment. Exogenous insulin can lower blood glucose effectively, but in this framework it does so by overriding substrate-driven prioritization and forcing glucose into storage pathways. That helps control symptoms while potentially increasing weight and lipid storage. GLP-1 receptor agonists can also improve glycemia, not necessarily because they correct insulin resistance, but because they reduce appetite, caloric intake, and metabolic load. Their success is entirely compatible with a substrate-overload model [20, 21].

7. Implications for Research and Clinical Practice

If the primary disturbance in type 2 diabetes is one of chronic substrate overload rather than intrinsic failure of insulin signaling, then treatment objectives should require redefinition. Rather than focusing primarily on overcoming presumed tissue resistance to insulin, therapeutic strategies would be expected to emphasize reduction of metabolic load, restoration of appropriate substrate balance, and prevention of ectopic lipid accumulation. In this context, improvements in glycemic control may be interpreted as the result of relieving metabolic pressure on key tissues rather than correcting a primary cellular defect.

Beyond these clinical considerations, if insulin resistance is primarily descriptive rather than primary, several implications for research follow. These implications are presented as logical extensions of the metabolic flux hypothesis rather than definitive clinical protocols. Research should place greater emphasis on temporal ordering: which abnormalities appear first, under what nutritional conditions, and in which tissues. Measures of lipid flux, ectopic fat, hepatic burden, postprandial substrate handling, and individual storage capacity may prove more causally informative than global indices that collapse diverse processes into the single language of resistance [8, 18].

Clinically, this perspective places dietary intervention at the center of therapy, not as an adjunct to pharmacologic management but as a primary means of reducing substrate burden. Improvement in glycemia following caloric restriction or reduction in refined carbohydrate intake may therefore be understood as a direct consequence of reduced metabolic load rather than restoration of impaired insulin signaling. Pharmacologic therapies remain important when they are targeted to alter substrate availability or redistribute nutrient flux.

8. Conclusion

The insulin resistance paradigm has become the default explanation for T2DM, but its conceptual authority exceeds its demon-

strated mechanistic foundation. It lacks a unifying coordinating mechanism across tissues, struggles to explain selective preservation of insulin's other functions, cannot readily account for the absence of broad parallel hormone resistance, and sits uneasily with transporter biology, rapid reversibility of hyperglycemia, lean diabetes, metabolically healthy obesity, and the extraordinary speed of the modern diabetes epidemic.

These difficulties do not eliminate the usefulness of the term insulin resistance as a descriptive shorthand. They do, however, cast doubt on its status as the primary causal engine of T2DM. A framework based on chronic substrate overload, limited metabolic capacity, and altered fuel selection offers a more parsimonious and biologically coherent explanation of many observations now attributed to insulin resistance. Reassessing the dominant paradigm may therefore be necessary if progress in prevention and treatment is to match the scale of the disease [18, 19, 20].

The next step should be to test these competing interpretations directly. Rather than asking only whether glucose disposal is reduced relative to insulin concentration, future work should ask what proximal metabolic events precede that change, whether elevations in fatty acid flux and ectopic lipid burden occur first, and whether reduction of substrate overload improves glycemia before any measurable alteration in canonical insulin-sensitivity indices. A framework that can explain timing, reversibility, tissue heterogeneity, and population trends with fewer ad hoc assumptions deserves serious consideration. If the observed phenotype of T2DM can be better explained by chronic nutrient excess and substrate competition than by a primary defect in insulin action, then the biological fallacy may lie not in the data, but in the interpretation that has long been imposed upon them [18, 19, 20].

REFERENCES

- [1] Parker ED, Lin J, Mahoney T, Ume N, Yang G, Gabbay RA, El-Sayed NA, Bannuru RR. Economic costs of diabetes in the U.S. in 2022. *Diabetes Care*. 2024;47(1):26-43. doi:10.2337/dci23-0085.
- [2] International Diabetes Federation. *IDF Diabetes Atlas*. 11th ed. Brussels: International Diabetes Federation; 2024.
- [3] Galicia-Garcia U, Benito-Villalvilla C, Jebari S, Larrea-Sebal A, Siddiqi H, Uribe KB, et al. Pathophysiology of type 2 diabetes mellitus. *Int J Mol Sci*. 2020;21(17):6275. doi:10.3390/ijms21176275.
- [4] Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF, Turner RC. Homeostasis model assessment: insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. *Diabetologia*. 1985;28(7):412-419. doi:10.1007/BF00280883.
- [5] DeFronzo RA, Tobin JD, Andres R. Glucose clamp technique: a method for quantifying insulin secretion and resistance. *Am J Physiol*. 1979;237(3):E214-E223. doi:10.1152/ajpendo.1979.237.3.E214.
- [6] Reaven GM. Banting lecture 1988. Role of insulin resistance in human disease. *Diabetes*. 1988;37(12):1595-1607. doi:10.2337/diab.37.12.1595.
- [7] Randle PJ, Garland PB, Hales CN, Newsholme EA. The glucose fatty-acid cycle. Its role in insulin sensitivity and the metabolic disturbances of diabetes mellitus. *Lancet*. 1963;281(7285):785-789. doi:10.1016/S0140-6736(63)91500-9.
- [8] Shulman GI. Ectopic fat in insulin resistance, dyslipidemia, and cardiometabolic disease. *N Engl J Med*. 2014;371(12):1131-1141. doi:10.1056/NEJMra1011035.
- [9] Petersen MC, Shulman GI. Mechanisms of insulin action and insulin resistance. *Physiol Rev*. 2018;98(4):2133-2223. doi:10.1152/physrev.00063.2017.
- [10] DeFronzo RA. From the triumvirate to the ominous octet: a new paradigm for the treatment of type 2 diabetes mellitus. *Diabetes*. 2009;58(4):773-795. doi:10.2337/db09-9028.
- [11] Thorens B. GLUT2, glucose sensing and glucose homeostasis. *Diabetologia*. 2015;58(2):221-232. doi:10.1007/s00125-014-3451-1.
- [12] Lim EL, Hollingsworth KG, Aribisala BS, Chen MJ, Mathers JC, Taylor R. Reversal of type 2 diabetes: normalisation of beta cell function in association with decreased pancreas and liver triacylglycerol. *Diabetologia*. 2011;54(10):2506-2514. doi:10.1007/s00125-011-2204-7.
- [13] Taylor R. Type 2 diabetes: etiology and reversibility. *Diabetes Care*. 2013;36(4):1047-1055. doi:10.2337/dc12-1805.
- [14] Eckel RH, Kahn R, Ferrannini E, Goldfine AB, Nathan DM, Schwartz MW, et al. Obesity and type 2 diabetes: what can be unified and what needs to be individualized? *J Clin Endocrinol Metab*. 2011;96(6):1654-1663. doi:10.1210/jc.2010-2235.
- [15] Kim JM, Kim HJ, et al. Rising prevalence of lean type 2 diabetes and comparison with overweight or obese type 2 diabetes. *BMC Public Health*. 2024;24.
- [16] Taylor R. Pathogenesis of type 2 diabetes: tracing the reverse route from cure to cause. *Diabetologia*. 2008;51(10):1781-1789. doi:10.1007/s00125-008-1116-7.
- [17] Polonsky KS. The past 200 years in diabetes. *N Engl J Med*. 2012;367(14):1332-1340. doi:10.1056/NEJMra1110560.
- [18] Poothullil J. A substrate-competition hypothesis for type 2 diabetes driven by nutrient excess rather than a primary insulin-signaling defect. *Med Hypotheses*. 2026;209. doi:10.1016/j.mehy.2026.111XXX.
- [19] Petersen KF, Dufour S, Befroy D, Lehrke M, et al. Reversal of nonalcoholic hepatic steatosis, hepatic insulin resistance, and hyperglycemia by moderate weight reduction in patients with type 2 diabetes. *Diabetes*. 2005;54(3):603-608. doi:10.2337/diabetes.54.3.603.
- [20] Corkey BE. Banting lecture 2011: hyperinsulinemia: cause or consequence? *Diabetes*. 2012;61(1):4-13. doi:10.2337/db11-1483.
- [21] Drucker DJ. Mechanisms of action and therapeutic application of glucagon-like peptide-1. *Cell Metab*. 2018;27(4):740-756. doi:10.1016/j.cmet.2018.03.001.



Multiple Myeloma with Unusual Hypopharyngeal Involvement: A Case Report

Article Record

Dr. Marco Briguglio^{§*}
*Corresponding Author



§ ENT clinic, Chivasso Hospital, Chivasso, It

RECEIVED

2026-03-14

ACCEPTED

2026-03-26

PUBLISHED

2026-04-04

PEER REVIEW

Double Blind

Abstract

Multiple myeloma is a blood cancer of monoclonal plasma cells that accumulate in the bone marrow and produce monoclonal immunoglobulin. Extramedullary involvement is rare at the time of initial multiple myeloma diagnosis (about 3,3% of all cases) and is generally associated with multiple relapses and poor prognosis. We present an extremely rare case of multiple myeloma with unusual hypopharyngeal involvement in an 83-year-old patient, who had a previous localization of plasmacytoma at the level of the cranial vault and was referred to our attention for a clinical picture of dysphonia persisting for approximately two years.

Multiple Myeloma

Hypopharynx

Extramedullary Disease

Dysphonia

Plasmacytoma

Otolaryngology

Hematologic Malignancy

AI USE STATEMENT

No generative AI was used for analysis or results.

FUNDING

No external funding was declared for this work.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

DATA AVAILABILITY

Not applicable for this article.

ETHICS

No ethics committee approval was required for this article type.

CONSENT

Not applicable for this article.

TRIAL REG.

Not applicable.

Crossref DOI: 10.34257/GJMRF254722

How to Cite: Briguglio (2026). Multiple Myeloma with Unusual Hypopharyngeal Involvement: A Case Report. Global Journal of Medical Research, 26(1), 19-21. DOI: 10.34257/GJMRF254722

LICENSE

© 2026 Global Journals. Open-access article under CC BY-NC-ND 4.0 International License.



Print ISSN 0975-5888



9 770975 588001

Online ISSN 2249-4618



9 772249 461010

Under the strict compliance and defined process of



METADATA CONTINUATION

AUTHOR CONTACT QR LEDGER

Dr. Marco Briguglio*



ARCHIVAL RECORD

Multiple Myeloma with Unusual Hypopharyngeal Involvement: A Case Report

Dr. Marco Briguglio^{§*}

§ ENT clinic, Chivasso Hospital, Chivasso, It

Abstract

Multiple myeloma is a blood cancer of monoclonal plasma cells that accumulate in the bone marrow and produce monoclonal immunoglobulin. Extramedullary involvement is rare at the time of initial multiple myeloma diagnosis (about 3,3% of all cases) and is generally associated with multiple relapses and poor prognosis. We present an extremely rare case of multiple myeloma with unusual hypopharyngeal involvement in an 83-year-old patient, who had a previous localization of plasmacytoma at the level of the cranial vault and was referred to our attention for a clinical picture of dysphonia persisting for approximately two years.

Keywords: Multiple Myeloma, Hypopharynx, Extramedullary Disease, Dysphonia, Plasmacytoma, Otolaryngology, Hematologic Malignancy

* Corresponding Author

Dr. Marco Briguglio

DOI

10.34257/GJMRF254722

1. Introduction

Multiple myeloma is the second most common haematological malignancy in high-income countries, and typically starts as asymptomatic precursor conditions—either monoclonal gammopathy of undetermined significance or smouldering multiple myeloma.

Multiple myeloma is a mature B-cell neoplasm defined by >10% of clonal plasma cells within bone marrow or biopsy-proven bony or EMP and it's complicated by organ dysfunction: hypercalcaemia, renal insufficiency, anaemia, and bone destruction (traditional CRAB features).

Multiple myeloma accounts for approximately 1% of all neoplastic diseases, with an incidence of 4.5–6 cases per 100,000 individuals and a median age at diagnosis of around 70 years.

A higher incidence has been reported in Western Europe, North America, and Australasia than in Asia and sub-Saharan Africa, which may be attributable to differences in diagnostic criteria and practices.

Risk factors for multiple myeloma include obesity, chronic inflammation, and exposure to pesticides, organic solvents, or radiation.

Inherited genetic variants also contribute to the development of multiple myeloma.

Advances in treatment, particularly the use of novel agents such as proteasome inhibitors, immunomodulatory drugs, and monoclonal antibodies targeting cell surface antigens, as well as high-dose therapy followed by autologous stem cell transplantation (ASCT) in younger patients, have markedly improved survival and overall outcomes in multiple myeloma.

2. Case presentation

We report the case of an 83-year-old patient who presented to the ENT clinic at Chivasso Hospital, in the province of Turin, for a two-year history of dysphonia. His medical history was notable for ascending aortic ectasia, hiatal hernia, and episodes of transient

global amnesia. Previous surgical history included multiple endoscopic procedures for nasal polyposis, a prior transurethral resection of the prostate (TURP) for prostatic adenoma, and hospitalization in 2017 for lumbar spondylodiscitis in the context of MSSA sepsis.

In autumn 2024, the patient developed a swelling of the cranial vault in the right parietal region and underwent a bone biopsy, which was consistent with a plasmacytic myeloma lesion exhibiting kappa light chain clonality.

A bone marrow biopsy confirmed myeloma infiltration of 30%, with IgG kappa plasma cells.

The patient underwent 10 sessions of radiotherapy targeting the cranial lesion.

During the ENT examination, oropharyngoscopy was unremarkable.

Flexible fiberoptic endoscopy revealed a neoplasm on the medial wall of the left piriform sinus, adjacent to the aryepiglottic fold, with apparently intact mucosa and no abnormal pattern on narrow-band imaging (NBI). Partial adduction of the left hemilarynx was observed, without macroscopic alterations in vocal cord mobility.

Contrast-enhanced neck CT confirmed the presence of a solid tissue mass measuring approximately 30 × 12 mm, obliterating the left piriform sinus and involving the ipsilateral thyroid cartilage, resulting in a lytic erosion. These findings were initially interpreted as consistent with a localization of the underlying disease.

Therefore, after a thorough informed discussion, the patient was scheduled for direct microlaryngoscopy with multiple biopsies of the hypopharyngeal lesion.

Approximately one month after the endoscopic evaluation, the patient underwent biopsy of the lesion under general anesthesia. Following placement of a rigid laryngoscope in suspension and under microscopic guidance, the previously noted exophytic, non-ulcerated, violaceous mass in the left piriform sinus was visualized, and multiple biopsy samples were obtained.

Microscopic analysis revealed hypopharyngeal mucosa associated with a fragment composed of numerous cells with abundant cytoplasm and round-to-oval nuclei exhibiting some irregularities. Immunohistochemical staining demonstrated a phenotype positive for CD79a and partially positive for CD38, while CD20 and CD30 were negative. Light chain restriction was observed, with an unbalanced expression of kappa light chains. The morphological and immunohistochemical findings were consistent with a localization of multiple myeloma.

The patient was referred back to the hematology team, and following interdisciplinary evaluation, initiation of hematologic therapy with a Velcade–Melphalan–Prednisone regimen was indicated.

3. Discussion

Multiple myeloma is a hematologic neoplasm characterized by the clonal proliferation of abnormal plasma cells within the bone marrow, leading to uncontrolled growth and potentially resulting in osteolytic bone lesions, renal impairment, anemia, and hypercalcemia. The median age at diagnosis is approximately 70 years, with nearly 63% of affected individuals being older than 65 years. In the vast majority of cases, multiple myeloma develops from pre-existing conditions known as monoclonal gammopathy of undetermined significance (MGUS) or smoldering multiple myeloma (SMM).

These precursors are characterised by the absence of signs or symptoms related to multiple myeloma or other lymphoproliferative diseases.

MGUS carries a risk of progression to symptomatic multiple myeloma of about 1–2% per year, with an estimated cumulative 20-year progression risk of approximately 18%.

Smoldering multiple myeloma (SMM) represents a more advanced premalignant plasma cell disorder, with an annual progression rate to overt multiple myeloma of roughly 10%.

The most common clinical manifestations of multiple myeloma include anemia (defined as hemoglobin <12 g/dL) in 73% of patients, osteolytic lesions on conventional radiographs in 79%, and elevated serum creatinine levels in 19%. Additional findings include hypercalcemia (13%), lymphadenopathy (1%), leukopenia (20%), and thrombocytopenia (5%).

At the time of multiple myeloma diagnosis, a thorough medical history, physical examination, and laboratory assessment should be performed. Evaluation of myeloma-related bone disease requires cross-sectional imaging.

Low-dose whole-body CT is recommended due to its rapid acquisition and greater sensitivity compared with conventional radiography. Current imaging guidelines also support the use of functional modalities, such as ¹⁸F-fluorodeoxyglucose (FDG) PET/CT or diffusion-weighted MRI, for treatment response assessment.

Bone marrow evaluation is necessary to quantify plasma cell infiltration, which can be assessed through histopathology of the biopsy specimen or by morphological and flow cytometric analysis of the aspirate.

Clinical outcomes in multiple myeloma are influenced by multiple factors, including intrinsic tumor cell characteristics (such as cytogenetic abnormalities, gene expression profiles, extramedullary involvement, and lactate dehydrogenase levels), tumor burden indicators (including β 2-microglobulin levels and thrombocytopenia), and patient-related factors, such as age, comorbidities, and overall frailty.

Proteasome inhibitors and immunomodulatory agents constitute the current cornerstone of multiple myeloma therapy and typically

serve as the standard backbone in clinical trials to which novel agents are added.

Corticosteroids, commonly dexamethasone or prednisolone, are consistently incorporated into treatment regimens. A fourth class of therapeutics, CD38-targeting monoclonal antibodies, has emerged as a critical component of both first-line and relapse-directed therapies.

Median overall survival among patients eligible for autologous stem cell transplantation is approximately 10 years, compared with 4–5 years in those who are not transplant candidates.

Extramedullary involvement is uncommon at the time of initial multiple myeloma diagnosis (about 3.3% of all cases) but occurs more frequently in patients with multiple relapses and is associated with a poor prognosis.

Extramedullary disease arises from hematogenous dissemination of malignant plasma cells and is characterized by the presence of soft tissue masses at extraosseous sites, such as the skin, lymph nodes, or brain, as well as pleural effusions or leptomeningeal involvement.

Extramedullary disease (EMD) may be detected either at initial diagnosis or during the course of the disease, particularly at relapse. Its occurrence is often associated with high-risk cytogenetic abnormalities and elevated serum lactate dehydrogenase (LDH) levels.

These factors contribute to a more refractory disease course, which is characterized by an increased risk of multiple relapses and diminished responsiveness to treatment.

Extramedullary disease is associated with a more aggressive clinical course, both at diagnosis and in the relapsed setting.

The management of extramedullary disease in multiple myeloma necessitates a personalized approach, with therapeutic strategies tailored according to the anatomical site, extent of disease dissemination, and underlying biological characteristics. Treatment varies depending on the location and burden of extramedullary involvement. In localized lesions, radiotherapy alone may be adequate, whereas in other cases, a combined approach incorporating both radiotherapy and surgical excision may be required.

When extramedullary involvement arises in the setting of systemic multiple myeloma, such as in the specific case we report, management generally involves systemic therapy using various combinations of anti-myeloma agents.

4. Conclusions

In the hypopharynx, squamous cell carcinoma remains the most frequent histological subtype, with approximately 84,000 new cases per year (2020 data).

Laryngeal involvement by multiple myeloma represents an extremely rare manifestation occurring within the context of systemic disease. Although cases of laryngeal plasmacytomas or laryngeal multiple myeloma have been described in the literature, hypopharyngeal localization appears to be a unique event. Based on the patient's clinical history and computed tomography findings, as well as the recent medical history—including the diagnosis of multiple myeloma involving the cranial vault in the preceding months—it could be hypothesized that the aerodigestive tract might represent a site of disease involvement. However, given the peculiarity of the case, the lesion was ultimately an incidental endoscopic finding.

The diagnosis was established by our pathology colleagues, and subsequent management was undertaken by the hematology team, who initiated a specific pharmacological treatment in light of the systemic nature of the disease. We therefore emphasize the crucial importance of interdisciplinary collaboration for the accurate

diagnostic assessment and appropriate therapeutic management of such complex cases.

Subject Index

acute scrotum, 6–7

bancroftian filariasis, 6–7

breast surgery, 1–5

caloric restriction, 15–19

caregiver stress, 8–14

chronic kidney disease, 8–14

Dysphonia, 20

ectopic fat, 15–19

end-stage renal disease, 8–14

Extramedullary Disease, 20

family caregivers, 8–14

filaria dance sign, 6–7

filarial orchitis, 6–7

filariasis, 6–7

gluconeogenesis, 15–19

glut2, 15–19

glut4, 15–19

Hematologic Malignancy, 20

hemodialysis, 8–14

hepatic glucose production, 15–19

histopathology, 1–7

hydrocele, 6–7

hyperglycemia, 15–19

Hypopharynx, 20

immunohistochemistry, 1–5

insulin resistance, 15–19

keratinizing carcinoma, 1–5

kingston caregiver stress scale, 8–14

mastectomy, 1–5

metabolic flux, 15–19

metaplastic breast tumor, 1–5

Multiple Myeloma, 20

neoadjuvant chemotherapy, 1–5

nutrient excess, 15–19

orchidectomy, 6–7

Otolaryngology, 20

parasitic infection, 6–7

pathophysiology, 15–19

personalized fat threshold, 15–19

Plasmacytoma, 20

primary breast carcinoma, 1–5

psychological burden, 8–14

quality of life, 8–14

rare breast neoplasms, 1–5

social support, 8–14

squamous cell carcinoma of the breast, 1–5

substrate overload, 15–19

testicular torsion, 6–7

testis, 6–7

torsion, 6–7

triple-negative pattern, 1–5

type 2 diabetes, 15–19

Author Guidelines

Comprehensive Guide to Publishing with GJMR

Global Journal of Medical Research | Open Access | Peer Reviewed | COPE Compliant

I. Our Commitment to Authors

The Global Journal of Medical Research (GJMR) is an internationally recognized, **open-access** academic journal dedicated to publishing high-quality, peer-reviewed research across the full breadth of medical science - including Neurology & Nervous System, Pharmacology & Drug Discovery, Microbiology & Pathology, Radiology & Diagnostics, Gynecology & Obstetrics, Diseases, Veterinary Science, Orthopedics, Surgery & Cardiovascular Medicine, Dentistry, Nutrition, and interdisciplinary medical studies.

GJMR is published by Global Journals Publishing Group Inc., indexed in major global academic databases, archived in leading digital repositories, and distributed to institutional subscribers worldwide in prestigious **hardbound volumes**.

We believe that the purpose of a medical journal is to amplify the voice of the clinician-researcher. Every operational decision we make is guided by a single principle: *the author should never be distracted from the science of healing*. Our professional editorial and production teams exist to handle every technical and logistical complexity so that you can devote your full energy to your medical research.

II. One-Click Submission: Publish Without the Hassle

GJMR has pioneered a **One-Click Submission** system designed to eliminate the traditionally burdensome process of paper submission.

A. Submit in Any Format

We accept manuscripts in **any common document format**, including but not limited to:

- Microsoft Word (.doc, .docx)
- Adobe PDF (.pdf)
- $\text{\LaTeX}$ source files (.tex)
- Rich Text Format (.rtf), Apple Pages, LibreOffice, or plain text

You do **not** need to install specialized software, learn $\text{\LaTeX}$, or adhere to a rigid template before submission. Simply write your clinical findings or research results in the format you are most comfortable with.

B. What You Need to Submit

To submit a manuscript, you only need to provide:

1. Your **full name**
2. Your **email address**
3. Your **manuscript file**

That is all. Submit directly via our portal at <https://globaljournals.org/submit-an-article/>.

Heading style: In the final typeset article, author-created headings are normally set in sentence case for readability. Fixed journal headings such as Abstract, Introduction, Materials and methods, Results, Discussion, Conclusion, References, and Acknowledgements are standardized by the production team. Acronyms, proper nouns, gene/species names, chemical notation, brand names, and Roman numerals are preserved.

C. What Happens After Submission

1. **Instant Confirmation:** You receive an automated email confirming receipt of your manuscript.
2. **Professional Formatting:** Our dedicated production executives convert your manuscript into our advanced internal $\text{\LaTeX}$ template - entirely on your behalf.
3. **Author Dashboard:** We create a secure account for you on the **Author Dashboard** and email your login credentials.
4. **Review Initiation:** Your professionally formatted, fully anonymized manuscript is assigned to expert medical reviewers through our rigorous double-blind peer-review process.

III. Rigorous Double-Blind Peer Review

Academic and clinical credibility is the cornerstone of GJMR. Every manuscript undergoes a **strict double-blind peer-review process** in which neither the authors nor the reviewers are aware of each other's identities.

A. The Review Workflow

1. **Desk Screening:** The editorial office performs an initial screening for scope, completeness, and adherence to ethical and clinical standards.
2. **Reviewer Assignment:** Two or more independent, domain-expert reviewers - specialists in your specific medical discipline - are assigned to evaluate your manuscript.
3. **Detailed Evaluation:** Reviewers assess the paper on criteria including clinical significance, originality, methodological rigor, statistical validity, patient safety implications, and presentation quality.
4. **Editorial Decision:** Based on reviewer recommendations, the Editorial Board renders one of three decisions: *Accept*, *Revise and Resubmit*, or *Decline*.

B. Complete Review Report & Research Assessment Sheet

Upon completion of the review, you will receive a **comprehensive Review Report** along with a detailed **Research Assessment Sheet**. These documents provide:

- Line-by-line reviewer comments keyed to **specific line numbers** in your typeset manuscript.
- A structured assessment covering originality, clinical significance, clarity, methodology, and overall quality.
- Constructive feedback and actionable suggestions for improvement.

C. Responding to Reviewer Comments

Addressing reviewer feedback is simple and flexible:

Option A - Author Dashboard: Log in, navigate to **Manage Submission**, and create a **support ticket** quoting line numbers from your review report.

Option B - Email: Send an email with a numbered list of corrections referencing the line numbers, along with your responses.

Important: You do **not** need to reformat the document yourself at any stage. Our production executives will implement all requested text changes directly.

IV. Publication Lifecycle: Complete Transparency

A. Early View (Galley Proof)

- Upon acceptance, a **galley proof** with **line numbers** is prepared for your final review.
- You may provide corrections by referencing specific line numbers via email or the Author Dashboard.

B. Ahead of Print

- Following the Early View, an **Ahead of Print** version is published before the final issue compilation.
- This version represents the final, corrected article but **does not yet include Volume or Issue numbers**.

C. Digital Publication (eJournal)

- After all corrections are finalized, the **digital eJournal edition** is published with line numbers removed.
- Your article receives its official DOI (**Digital Object Identifier**) and is indexed across global academic databases.
- The article becomes freely and permanently accessible online under our open-access policy.

D. Hardbound Print Publication

- Approximately **15 days after digital publication**, your research is printed in **premium hardbound volumes** and distributed to medical libraries, teaching hospitals, and institutional subscribers worldwide.
- The corresponding author receives a **complimentary hardbound copy** dispatched via government courier at no additional cost.

V. Advanced Technology & AI-Enabled Research Broadcasting

A. Multi-Format Native Publication

Every accepted article is published natively across multiple formats:

- **Interactive Digital eJournals** optimized for all devices.
- **Premium Hardbound Print Editions** for institutional archives and clinical reference libraries.
- **Machine-Readable XML & HTML** for web accessibility and medical database indexing.

B. AI-Powered Discoverability & SEO

Our proprietary AI systems automatically tag, categorize, and optimize article metadata for maximum search engine visibility, ensuring your medical research reaches clinicians, scientists, and healthcare professionals worldwide.

VI. Ethics, Integrity & COPE Compliance

GJMR maintains the highest standards of publication ethics, guided by the principles of the **Committee on Publication Ethics (COPE)** and relevant medical research ethics frameworks.

- All submissions are screened using state-of-the-art plagiarism detection software.
- Authors must disclose all funding sources, conflicts of interest, and clinical trial registration numbers.
- Research involving human subjects must include ethical approval from a recognized Institutional Review Board (IRB) and confirmation of informed consent.
- Animal research must comply with established guidelines for humane treatment.
- Our comprehensive, enhanced COPE-based ethical publishing guidelines are available in detail at <https://globaljournals.org>.

VII. Perpetual Archiving & Geo-Distributed Data Infrastructure

Your published research is **redundantly archived across multiple geographically distributed data centers** spanning several continents, including advanced **deep-sea data center facilities** engineered for unparalleled resilience and longevity. This guarantees **lifetime hosting**, disaster resilience, and immutable DOI resolution for every published article.

VIII. Open Access: Free Knowledge for All

GJMR is a Fully Open Access Journal.

Every article published in GJMR is **freely and permanently available online** from the moment of publication - accessible to clinicians, researchers, medical students, and the general public worldwide **without any subscription fees, paywalls, or access restrictions**. Open access to medical knowledge saves lives.

Accepted articles are published under the **Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International (CC BY-NC-ND 4.0)** license. Authors retain full copyright.

IX. The L^AT_EX Author Package (Entirely Optional)

Reading or using the L^AT_EX Author Package is entirely optional.

Simply send us your manuscript in Word, PDF, or any other format. Our production team will expertly convert it into our advanced typesetting system. **You do not need to learn or install anything.**

Contact & Support

Submission Portal: <https://globaljournals.org/submit-an-article/>

Website: <https://globaljournals.org>

Email: helpdesk@globaljournals.org

*At GJMR, your research advances the science of healing.
We handle the complexities of publishing so you can focus
on what matters most - improving patient outcomes.*

GLOBAL JOURNAL

of Medical Research: F

Diseases

globaljournals.org



Save our Planet



Online ISSN 2249-4618



9 772249 461010