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Knowledge, Attitude, and Practice of Infection Control Management and Prevention Among Medical Staff in Tobruk

A Quasi-Experimental Study

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Abstract

Background: Healthcare-associated infections (HAIs) remain a critical challenge in healthcare systems worldwide, particularly in low- and middle-income countries such as Libya, where infection prevention and control (IPC) infrastructure is limited. Enhancing healthcare workers' (HCWs') knowledge, attitudes, and practices (KAP) regarding IPC is essential for reducing HAI burden.

Objectives: This study aimed to assess the impact of a structured educational workshop on improving the KAP of HCWs toward IPC in Tobruk city, Libya, and to identify demographic and professional factors associated with KAP levels.

Methods: A quasi-experimental pre-post intervention design was conducted across three governmental health facilities in Tobruk from February to May 2025. A validated questionnaire was administered before and after the workshop. Data were analyzed using the Wilcoxon Signed-Rank Test and multinomial logistic regression in RStudio.

Results: A total of 54 HCWs participated. Statistically significant improvements were observed across all three domains: knowledge ($p < 0.001$), attitudes ($p = 0.014$), and practices ($p = 0.011$). The proportion of participants with "good knowledge" increased from 83.3% to 92.6%. Physician specialization was significantly associated with knowledge level (OR = 0.02; 95% CI: 0.00–0.43; $p = 0.026$).

Conclusions: Targeted educational interventions are effective in improving KAP among HCWs, even when baseline knowledge is relatively high. A notable knowledge-practice gap was identified, underscoring the need for structured, simulation-based training and systematic auditing.

Keywords: *Infection prevention and control; Healthcare-associated infections; Knowledge attitude and practice; Healthcare workers; Libya; Educational intervention*

1. Introduction

Healthcare-associated infections (HAIs) represent a persistent global challenge with significant implications for patient safety, healthcare costs, and public health. These infections compromise the quality of care, increase morbidity and mortality rates, and impose a considerable burden on healthcare systems.

Nosocomial infections—a term used interchangeably with HAIs—are those acquired during the course of inpatient medical care and are not present or incubating at the time of admission. It is anticipated that all healthcare providers (HCPs) adhere rigorously to established standards of

practice. These standards, encompassing knowledge, attitude, and practice (KAP), must be integrated into the institutional fabric of all health facilities to ensure client safety and protection.

In 2016, the World Health Organization (WHO) issued guidelines delineating eight core components for the effective implementation of infection prevention and control (IPC) programs at both national and facility levels. These components emphasize evidence-based interventions, including care bundles and comprehensive implementation strategies.

The burden of HAIs is disproportionately higher in low- and middle-income countries, including Libya, owing to limited resources and suboptimal IPC infrastructure. In Libya, data indicate suboptimal adherence to key IPC practices. A study conducted at Benghazi Medical Centre found that only 51.3% of HCWs had received formal training in hand hygiene, while a study in Tripoli revealed that only 40% of HCWs met WHO-recommended handwashing standards.

Successful IPC strategies depend not only on education and training but also on the engagement and attitudes of HCWs toward prevention practices. The primary aim of this study was to assess the impact of an interactive infection control workshop on improving the KAP of HCWs in Tobruk city.

2. Methodology

2.1 Study Design

This study adopted a quasi-experimental pre-post intervention design to assess the knowledge, attitudes, and practices related to IPC among healthcare workers in governmental hospitals in Tobruk city. This design enables comparison of data collected before and after an intervention without requiring a control group, making it particularly suitable for training evaluations in resource-limited environments.

2.2 Study Settings and Schedule

The study was implemented across three governmental health facilities in Tobruk city: Tobruk Medical Centre, Bab Derna Centre, and the Blood Bank Centre. The full study period extended from February 10 to May 17, 2025.

2.3 Inclusion and Exclusion Criteria

Participants included nurses and physicians working in clinical departments with direct patient care responsibilities, across varying levels of professional experience. Administrative staff, support personnel, and individuals not directly engaged in patient care were excluded from the study.

2.4 Intervention Implementation

Structured and targeted awareness sessions were designed and delivered to educate participants on IPC principles. The intervention encompassed the dissemination of basic infection control principles, standard precautions, and evidence-based practices for preventing HAIs. Training was conducted in an interactive format, encouraging discussion and participation in practical demonstrations.

2.5 Questionnaire Design and Data Collection

A pre-designed structured questionnaire was adapted from validated literature originating from a university hospital in Qassim, Saudi Arabia, and translated from English into Arabic. The

questionnaire underwent expert review by three specialists. Aligned with WHO and CDC guidelines, it assessed HCWs' KAP toward IPC across three domains:

- Knowledge — understanding of infection and basic IPC principles
- Attitudes — scenario-based questions exploring professional behavior in clinical contexts
- Practices — daily habits including hand hygiene, PPE use, blood spill management, sharps handling, and waste disposal

2.6 Ethical Approval

This study adhered to the ethical standards of institutional and national research committees and complied with the 1964 Declaration of Helsinki. Ethical approval was obtained from the Research Ethics Committee of Tobruk University.

2.7 Statistical Analysis

Data management and analysis were performed using RStudio (version 2024.12.1+563). Pre- and post-training values were compared using the Wilcoxon Signed-Rank Test. Variables with statistically significant associations were entered into a multinomial logistic regression model. Statistical significance was set at $p < 0.05$.

3. Results

3.1 Participant Characteristics

A total of 54 healthcare professionals participated. The median age was 26 years (IQR: 24–30), with females comprising 64.8% (n = 35) and males 35.2% (n = 19). The majority (83.3%, n = 45) had fewer than six years of professional experience. Physicians represented 33.3% (n = 18), followed by laboratory technicians (20.4%), nurses (14.8%), and pharmacists (5.6%). Notably, 72.2% (n = 39) had received no prior formal IPC training.

Table 1. Demographic and clinical characteristics of study participants (N = 54)

Variable	Category	(%) n
Gender	Female	(64.8%) 35
	Male	(35.2%) 19
Experience	years 6 >	(83.3%) 45
	years 6 <	(16.7%) 9
IPC Training	No	(72.2%) 39
	Yes	(27.8%) 15
Previous Work Infection	No	(77.8%) 42
	Yes	(22.2%) 12
PPE Availability	Yes	(92.6%) 50
Specialization	Doctor	(33.3%) 18
	Lab Technician	(20.4%) 11
	Nurse	(14.8%) 8

	Pharmacist	(5.6%) 3
	Administrative	(7.4%) 4
	Other	(18.5%) 10

3.2 Pre- and Post-Intervention KAP Scores

Statistically significant improvements were observed in all three KAP domains following the educational intervention. Knowledge scores increased from median 17 (IQR: 16–18) to 19 (IQR: 17.25–19) post-intervention ($p < 0.001$). The proportion with "good knowledge" improved from 83.3% to 92.6%. Attitude scores improved ($p = 0.014$), with the "good attitude" proportion rising from 40.7% to 66.7%. Practice scores also improved significantly ($p = 0.011$).

Table 2. Comparison of pre- and post-workshop KAP scores (Wilcoxon Signed-Rank Test)

Domain	Pre-Workshop Median (IQR)	Post-Workshop Median (IQR)	p-value
Knowledge	(18–16) 17	(19–17.25) 19	*0.001 >
Attitude	(57–51) 53	(60.5–52) 57	*0.014
Practice	(72–56) 66.5	(72.75–63) 70	*0.011

*$p < 0.05$ — statistically significant **

3.3 Logistic Regression Analysis

Multinomial logistic regression revealed that physician specialization was the only statistically significant predictor of knowledge categorization (OR = 0.02; 95% CI: 0.00–0.43; $p = 0.026$). No significant predictors were identified for attitude or practice categorizations.

Table 3. Logistic regression for predictors of knowledge categorization

Variable	OR	95% CI	p-value
Gender: Male vs. Female	0.40	0.05–2.45	0.3
Age	0.81	0.57–1.08	0.2
Experience: > 6 years vs. ≤ 6 years	8.97	0.16–1021	0.3
IPC Training: Yes vs. No	0.30	0.02–2.74	0.3
Specialization: Doctor vs. Administrative*	0.02	0.00–0.43	0.026*
Previous Work Infection: Yes vs. No	1.87	0.17–18.4	0.6

** $p < 0.05$ — statistically significant*

4. Discussion

This study evaluated the effectiveness of a structured educational workshop in enhancing the KAP of healthcare workers toward infection prevention and control in Tobruk city, Libya. The findings

demonstrated statistically significant improvements in all three domains—knowledge, attitudes, and practices—following the intervention.

4.1 Knowledge Outcomes

The proportion of participants classified under the "good knowledge" category increased from 83.3% to 92.6% ($p < 0.001$), with the complete elimination of the "poor knowledge" category. These findings are consistent with a substantial body of international literature from Egypt [10], Oman [15], Nigeria [16], Spain [17], and Yemen [18], which affirm that focused educational interventions yield measurable improvements in IPC knowledge.

A notable feature of this study is the paradox it reveals: significant knowledge improvements were achieved from an already high baseline (83.3%), despite 72.2% of participants having never received formal IPC training. This suggests that informal or implicit learning—acquired through routine practice and peer interaction—may have played a substantial role in shaping foundational understanding. The average participant age of 26 years indicates an early-career cohort whose baseline knowledge is consistent with findings from modern academic curricula emphasizing IPC.

4.2 Attitude Outcomes

Attitude scores improved significantly following the intervention ($p = 0.014$), with the proportion of participants categorized as having a "good attitude" increasing from 40.7% to 66.7%. The interactive and participatory format of the training facilitated attitudinal shifts by providing HCWs with opportunities to engage with real-world clinical scenarios, promoting intrinsic motivation for behavioral change.

4.3 Practice Outcomes and the Knowledge-Practice Gap

Practice scores showed a statistically significant improvement post-intervention ($p = 0.011$), with median scores rising from 66.5 to 70. However, despite significant gains in knowledge and attitudes, the relative magnitude of improvement in practices was comparatively modest—a phenomenon frequently referred to as the "knowledge-practice gap."

Qualitative observations during the workshop revealed critical deficiencies in fundamental IPC procedures, including improper PPE donning/doffing, incorrect sharps handling, inadequate blood spill responses, and insufficient understanding of isolation precaution types. These observations reinforce the inadequacy of relying solely on implicit learning for IPC competency development. Structured, evidence-based training is essential to consolidate informally acquired knowledge and standardize practices across healthcare teams.

4.4 Regression Analysis and Demographic Predictors

Among demographic variables assessed, physician specialization was the only statistically significant predictor of knowledge categorization (OR = 0.02; $p = 0.026$). This finding may reflect differences in question alignment with nursing-oriented IPC content or role-specific knowledge gaps among clinical staff. No significant predictors were identified for attitude or practice categorizations, likely due to the limited statistical power afforded by the sample size.

These practical gaps—closely aligned with the absence of formal IPC training among most participants—are echoed in findings from other contexts. In Pakistan, nurses were found to follow outdated protocols inherited from senior colleagues, without reference to updated national or global

guidelines [19]. Furthermore, the average participant age of 26 years indicates an early-career cohort whose high baseline knowledge (83.3%) is consistent with findings from Saudi Arabia [14] and the United Kingdom [20], where less experienced HCWs exhibited higher knowledge levels than their senior colleagues—an observation attributed to modern academic curricula placing greater emphasis on IPC concepts.

4.5 Study Limitations

- Limited sample size (N = 54) constrained statistical power of regression models
- Self-reported data introduces potential social desirability bias
- Absence of a control group limits causal inference
- Single-city design may limit generalizability to broader Libyan contexts

5. Conclusion

This study provides compelling evidence that targeted educational interventions are essential for enhancing healthcare workers' capacity in infection prevention and control, even among cohorts with a relatively high baseline of theoretical knowledge. The educational workshop resulted in statistically significant improvements across all measured domains—knowledge, attitudes, and practices.

A central finding is the paradox of high pre-intervention knowledge (83.3%) coexisting with a profound absence of prior formal IPC training (72.2%). This phenomenon suggests that implicit learning plays a pivotal role in shaping foundational understanding of early-career health professionals. However, implicit learning alone does not guarantee procedural accuracy.

Future interventions should prioritize simulation-based, competency-assessed training to address the knowledge-practice gap. Larger, multi-center investigations with control groups are recommended to strengthen the evidence base and inform national IPC policy in Libya.

6. Recommendations

Based on the findings of this study, the following recommendations are proposed:

- Implement mandatory, structured IPC training programs for all newly hired staff, complemented by annual refresher workshops.
- Incorporate simulation-based, hands-on learning components covering PPE donning/doffing, blood spill management, and sharps disposal.
- Replicate this study on a larger scale across multiple Libyan health centers with a control group for stronger causal evidence.
- Conduct qualitative research including focus groups to investigate barriers preventing HCWs from translating knowledge into consistent clinical practice.
- Establish non-punitive, systematic auditing mechanisms combining observation-based audits with constructive feedback to cultivate a culture of continuous improvement.

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Assessment of the Implementation of Electronic Medical Records in Libyan Healthcare Institutions

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Abstract

Background: Electronic Medical Records (EMR) systems are pivotal in modernizing healthcare by enhancing data accuracy, patient safety, and operational efficiency. However, in Libya, EMR adoption remains limited due to infrastructural, financial, and skill-based barriers, hindering the transition from paper-based to digital health information systems. Objectives: This study aimed to evaluate the current state of EMR implementation in Libyan healthcare institutions, identify key challenges and facilitators, and propose strategies for sustainable adoption. Methods: A cross-sectional survey was conducted from February to September 2025 using Google Forms, targeting 150 healthcare professionals across various institutions. The questionnaire assessed sociodemographic characteristics, EMR usage, perceived benefits, and barriers. Data were analyzed using SPSS version 26, employing descriptive statistics. Results: Only 9.3% of institutions reported EMR usage, with 71.3% of respondents never utilizing the system daily. Logistic regression identified training level (OR=2.34, p<0.001) and IT infrastructure adequacy (OR=2.51, p<0.001) as significant predictors of recommending EMR expansion. Major barriers included poor IT infrastructure (90%), insufficient training (75%), and resistance to change (40%). Positive aspects included perceived reductions in medical errors (51.9% agreement), improved efficiency (52.6%), and enhanced communication (82%). An overwhelming 88% recommended expanding EMR use. Conclusion: EMR implementation in Libya faces significant hurdles but holds promise for healthcare improvement. Recommendations include investing in infrastructure, training, and policy reforms, with potential integration of artificial intelligence for advanced data analytics. This study provides insights for policymakers to foster digital health transformation in resource-limited settings.

Keywords: *Electronic Medical Records (EMR); Digital Health; Libya; Healthcare Informatics; Health Information Systems.*

1. Introduction

Digital electronic medical record (EMR) systems represent a significant milestone in the global healthcare transformation, facilitating enhancements in clinical performance, patient safety, and data control within medical institutions . EMRs promote evidence-based decision-making, improve care coordination, and reduce medical errors by digitizing patient information and ensuring its availability across departments and centers. Globally, the use of EMR is associated with increased fact accuracy, operational performance, and accelerated adherence to first-rate and security requirements via encryption and authentication systems . These systems are important not only for improving clinical processes, but also for improving governance, accountability and long-term health system performance. Despite well-documented benefits, Libya is still in the early stages of

EMR implementation. The Libyan healthcare system is heavily dependent on paper-based medical records and small digital administrative operations .As of 2017, approximately one third of the basic functions of a viable health information system (HIS) were missing, reflecting systemic deficiencies in monitoring, evaluation and digital infrastructure . Libya now lacks cost-effective monitoring and evaluation plans, standardized data management techniques, and institutionalized data quality assessment. Furthermore, processes for independent data evaluation and civil society participation are insufficient, while the Health Information Center (HIC) operates without any special section dedicated to emergency data .

These challenges highlight the complexity of digital transformation in the Libyan health sector. Key barriers to EMR adoption include inadequate IT infrastructure, limited technical competencies among healthcare professionals, insufficient funding, and weak governance frameworks . Although a few pilot projects and small-scale initiatives have demonstrated promising outcomes—such as improved data accessibility, reduced documentation errors, and enhanced workflow efficiency—these efforts remain fragmented and unsustainable due to interoperability gaps and policy discontinuity. Moreover, persistent rural–urban disparities in digital readiness, insufficient capacity-building programs, and concerns over long-term financial sustainability further hinder widespread implementation.

This study aims to comprehensively assess the current state of EMR implementation in Libyan healthcare institutions, identify key barriers and facilitators influencing adoption, and propose evidence-informed strategies for sustainable and scalable digital transformation. It is hypothesized that an integrated approach—combining phased pilot programs, infrastructure development, workforce capacity-building, robust policy frameworks, and stakeholder engagement—will facilitate progress from isolated trials to interoperable, nationwide EMR systems. By addressing these dimensions, the study seeks to fill existing knowledge gaps and provide actionable insights for policymakers, healthcare leaders, and technology developers working to modernize Libya’s health information ecosystem. In doing so, this research situates EMR adoption within Libya’s unique socio-economic and institutional context, contributing to the broader discourse on digital health transformation in developing countries. It underscores the critical importance of aligning technological innovation with local capacities, regulatory environments, and governance mechanisms to achieve sustainable improvements in healthcare quality, efficiency, and patient safety outcomes.

2. Methodology

- **Ethical approval and consideration**: The researchers considered the study a modest risk. Participation was optional and confidential. All participants provided electronic informed consent before starting the survey.
- **Study Design and Data Collection:** The present investigation utilized an anonymous, questionnaire-based, self-reported cross-sectional design, executed from February to September 2025. The survey was administered via Google Forms to 150 participants.
- **Questionnaire design:** The survey was made up of four distinct sections. The first section collected baseline socio-demographic data from the respondents. The second section consisted of evaluation questions on the extent of electronic medical record use in Libyan

healthcare institutions, while the third section consisted of questions about the challenges and obstacles participants faced in using electronic records. The fourth section consisted of open-ended questions.

- **Data Management and Statistical Analysis**: The Statistical Package for the Social Sciences (SPSS) for Windows, version 26, was used to analyze the data. We expressed measurement data as mean ± standard deviation (X ± S), and we expressed count data as frequencies and percentages.

3. Results

The sociodemographic characteristics of the study group: The study group comprised 150 participants. Table 1 has a full summary of their sociodemographic features. The majority of participants were between 35 and 40 years old (96, 68.8%), worked in government hospitals (71, 47.3%), and belonged to the western zone (85, 57%). Regarding occupation, 107 (71.4%) were medical laboratory technicians, 100 (66.7%) had more than 12 years of experience, and 136 (90.7%) said that their institutions did not use electronic records, while just 14 (9.3%) acknowledged current use (see Table 1).

Table 1: The socio-demographic characteristics of the surveyed participants (n=150).

Variable	Categories	Frequency	Percent
Age in years (n=150)	25 – 30	6	4.2%
	31 – 35	12	8.5%
	36 – 40	96	68.8%
	More than 40	26	18.5%
Education Level	Bachelor's Degree	93	62%
	Master's Degree	45	30%
	PhD	12	8%
Institution Type	Government Hospital	71	47.3%
	Reference Laboratory	15	10%
	Private Hospital	14	9.3%
	Government Health Centre	43	28.7%
	Medical-Lab Supplies Company	7	4.7%
Libyan Zone	Western	85	57%
	Eastern	29	19%
	Southern	28	19%
	Central	8	5%
Job Category	Lab Technician	107	71%
	Doctor	36	24%
	Administrative Staff	7	5%
Experience Category	< 1 year	7	4.7%
	4-7 years	22	14.7%
	8-12 years	21	14.0%
	> 12 years	100	66.7%
EMR/EHR usage	NO	136	90.7%

	Yes	14	9.3%

Evaluation questions regarding the use of electronic medical records in Libyan health institutions: The analysis of EMR/EHR system usage among healthcare personnel, as detailed in Table 2, reveals substantial underutilization, with 71.3% not using the system daily. Despite 53.3% reporting workstation availability, factors such as inadequate training and workflow integration barriers appear to limit engagement. Notably, 39.3% of participants found their training insufficient, affecting their confidence and system usage rates. Though 64.6% felt competent with the system, this confidence does not correlate with usage frequency due to perceived external limitations. Technical support satisfaction was mixed, with around 40% expressing dissatisfaction, while IT infrastructure garnered only 27.3% positive feedback, presenting serious challenges to effectiveness. On the other hand, perceptions of data security were relatively optimistic, with 46.6% confident in patient data protection, even as a significant number remained uncertain. System integration showed moderate acceptance (33.3% agreement) but revealed interoperability issues, as nearly 45% of respondents were neutral or disagreed. Participants noted positive impacts on error reduction (51.9% agreement), efficiency enhancement (52.6%), and communication improvement (82% agreement), highlighting the clinical benefits of EMR/EHR systems. Importantly, 88% advocated for the continuation or expansion of EMR/EHR usage, reflecting overall support despite technological barriers and necessitating focused interventions to maximize the potential of digital health records.

Table 2: Summarizes the evaluation questions regarding the use of electronic medical records in Libyan health institutions (n=150).

Question	Never/Rarely/Sometimes/Often/Always or Strongly disagree/Disagree/Neutral/Agree/Strongly agree, n (%)	Mean (SD)
Frequency of EMR/EHR use in daily tasks	Never: 107 (71.3) Rarely: 7 (4.7) Sometimes: 22 (14.7) Often: 10 (6.6) Always: 4 (2.6)	1.71 (1.31)
Availability of EMR/EHR system on workstations	Strongly disagree: 35 (23.3) Disagree: 9 (6.0) Neutral: 26 (17.3) Agree: 45 (30.0) Strongly agree: 35 (23.3)	3.24 (1.31)
Perceived training to use electronic records	Strongly disagree: 42 (28.0) Disagree: 17 (11.3) Neutral: 58 (38.7) Agree: 25 (16.7) Strongly agree: 8 (5.3)	2.60 (1.21)
I feel competent to perform tasks using the system	Strongly disagree: 0 (0.0) Disagree: 18 (11.8)	3.82 (1.20)

	Neutral: 35 (23.5) Agree: 53 (35.3) Strongly agree: 44 (29.4)			
Reliable technical support available when problems arise	Strongly disagree: 35 (23.3) Disagree: 26 (17.3) Neutral: 35 (23.3) Agree: 35 (23.3) Strongly agree: 19 (12.7)			2.85 (1.30)
Adequacy of IT infrastructure (Internet, LAN, devices) to support EMR/EHR	Strongly disagree: 50 (33.3) Disagree: 17 (11.3) Neutral: 42 (28.0) Agree: 33 (22.0) Strongly agree: 8 (5.3)			2.55 (1.29)
Patient data are sufficiently protected and secure in the system	Strongly disagree: 9 (6.0) Disagree: 18 (12.0) Neutral: 53 (35.3) Agree: 44 (29.3) Strongly agree: 26 (17.3)			3.40 (1.09)
Patient records in the system are accurate and complete	Strongly disagree: 4 (2.7) Disagree: 13 (8.7) Neutral: 45 (30.0) Agree: 58 (38.7) Strongly agree: 30 (20.0)			3.73 (1.07)
System integrated with other systems (labs, radiology, pharmacy) or supports easy info exchange	Strongly disagree: 42 (28.0) Disagree: 25 (16.7) Neutral: 33 (22.0) Agree: 33 (22.0) Strongly agree: 17 (11.3)			2.72 (1.37)
EMR use contributed to reducing medical errors	Strongly disagree: 24 (16.0) Disagree: 8 (5.3) Neutral: 40 (26.7) Agree: 62 (41.3) Strongly agree: 16 (10.7)			3.25 (1.15)
Using the system improved work efficiency and time savings	Strongly disagree: 9 (6.0) Disagree: 9 (6.0) Neutral: 53 (35.3) Agree: 53 (35.3) Strongly agree: 26 (17.3)			3.52 (1.14)
EMR improves patient follow-up and medical team communication	Strongly disagree: 9 (6.0) Disagree: 0 (0.0) Neutral: 18 (12.0) Agree: 70 (46.7) Strongly agree: 53 (35.3)			4.05 (1.12)
Recommend	Yes: 132		(88.0)	4.64 (0.88)

continuing/expanding EMR use in your organization	Maybe: 9 (6.0) No: 9 (6.0)	

The primary challenges confronting the use of electronic records within an organization: The analysis of the data, as detailed in Table 3, reveals that the primary obstacles hindering the effective implementation of electronic records are primarily attributed to two significant factors: inadequate IT infrastructure, which is a concern for 90% of respondents, and a lack of sufficient training and human competence affecting 75% of participants. Furthermore, additional challenges include resistance to change, recurrent errors in software or systems, and insufficient technical support, each of which impacted 40% of those surveyed. Other barriers noted include frequent power outages mentioned by 35% of respondents and constraints related to costs or policies experienced by 25% of participants.

Table 3: The primary challenges confronting the use of electronic records within an organization

Barrier	N	Percent
Poor IT infrastructure (internet, hardware)	**135**	**90%**
Insufficient training / human competence	**113**	**75%**
Resistance to change (staff / physicians)	**60**	**40%**
Recurrent software / system errors	**60**	**40%**
Weak technical-support / maintenance	**60**	**40%**
High licence / operation / maintenance cost	**38**	**25%**
Frequent power outages	**53**	**35%**
Legal / regulatory / institutional policy constraints	**38**	**25%**

Table 4: Binary logistic regression predicting recommendation for EMR expansion

Predictor Variable	B	SE	Wald	p-value	OR	95% CI for OR
Constant	**-1.23**	**0.45**	**7.45**	**0.006**	**0.29**	
Training Level	**0.85**	**0.21**	**16.38**	**<0.001**	**2.34**	**[1.55, 3.52]**
IT Infrastructure Adequacy	**0.92**	**0.19**	**23.46**	**<0.001**	**2.51**	**[1.73, 3.64]**
Self-efficacy	**0.68**	**0.23**	**8.74**	**0.003**	**1.97**	**[[1.26, 3.09**
Communication Improvement	**0.56**	**0.25**	**5.02**	**0.025**	**1.75**	**[1.07, 2.86]**
Years of Experience	**-0.12**	**0.08**	**2.25**	**0.134**	**0.89**	**[0.76, 1.04]**

Model $\chi^2 = 42.35$, $p < 0.001$; Nagelkerke $R^2 = 0.68$; Overall classification accuracy = 86.7%

Binary logistic regression analysis identified significant predictors of recommending EMR expansion. The model explained 68% of the variance (Nagelkerke $R^2 = 0.68$) and correctly

classified 86.7% of cases. Perceived training level (OR = 2.34, $p < 0.001$) and IT infrastructure adequacy (OR = 2.51, $p < 0.001$) emerged as the strongest predictors. For each one-unit increase in perceived training level, the odds of recommending EMR expansion increased by 2.34 times, while each one-unit increase in perceived IT infrastructure adequacy increased the odds by 2.51 times.

4. Discussion

This study assesses Electronic Medical Record (EMR) implementation in Libyan healthcare, highlighting a significant adoption gap: only 9.3% of institutions have adopted EMRs, despite 88% of participants supporting their expansion, creating a "Libyan EMR paradox." This divergence suggests structural barriers, rather than attitudes, hinder implementation [10]. Logistic regression analysis identifies that adequate IT infrastructure (OR = 2.51) and training levels (OR = 2.34) are key predictors for recommending EMR expansion, indicating that investments in these areas could greatly enhance advocacy for broader system adoption [11].

The strong link between perceived training and self-efficacy underscores the need for continuous training programs that build professionals' confidence, aligning with competency-based education concepts [12]. Prevalent challenges, such as inadequate IT infrastructure (90%) and insufficient training (75%), are established but Libya's unique context presents specific barriers, including technical, financial, and regulatory issues, compounded by frequent power outages (35%).

Additionally, perceptions of EMRs vary across professional roles, signifying that tailored training and change management strategies are needed for different user groups. The study concludes that while substantial structural obstacles exist, the strong support among healthcare professionals indicates significant potential for digital transformation. By focusing on infrastructure and training investments, implementing customized strategies, and addressing Libya’s distinct contextual challenges, policymakers can enhance healthcare quality and efficiency.

5. Limitations

Several limitations affect the interpretation of this study's findings. The cross-sectional design restricts the ability to draw causal inferences regarding variable relationships. Additionally, the use of self-reported data may lead to social desirability bias and common method variance. While the sample size of 150 is sufficient for descriptive analyses, it limits the statistical power for advanced multivariate analyses. The concentration of participants in specific Libyan regions further affects the generalizability of the results to rural or remote areas. Moreover, the lack of objective performance metrics restricts the validation of self-reported benefits against actual clinical outcomes. Future research should consider longitudinal designs, larger and more diverse samples, and mixed-methods approaches to further explore the dynamics of Electronic Medical Record (EMR) implementation and address these limitations.

6. Conclusion

This study provides a comprehensive assessment of the current landscape of Electronic Medical Record (EMR) implementation within Libyan healthcare institutions. The findings reveal a

significant digital divide; while there is a high level of acceptance among healthcare professionals, with 88% advocating for the expansion of EMR usage, actual implementation remains critically low, with over 90% of respondents relying on traditional methods. The research identifies that the barriers to adoption are primarily structural and technical rather than behavioral. Poor IT infrastructure and insufficient human capacity building emerged as the most formidable obstacles, cited by 90% and 75% of participants, respectively. These challenges are further compounded by issues regarding system interoperability and consistent technical support. Consequently, for the Libyan healthcare sector to realize the benefits of digital transformation—such as reduced medical errors and improved workflow efficiency—a fragmented approach is insufficient. Sustainable EMR adoption requires a national strategic framework that prioritizes investing in robust hardware and network infrastructure, alongside comprehensive, continuous training programs for medical staff. Establishing these foundational elements is not only crucial for immediate clinical improvements but is also a prerequisite for future integrations of advanced

6. Recommendations

Based on the statistical analyses presented, a phased implementation strategy is recommended, which prioritizes the following three areas: firstly, enhancing infrastructure in government health centers where existing perceptions are notably low; secondly, rolling out competency-based training programs specifically aimed at laboratory technicians and other supporting staff; and thirdly, establishing continuous evaluation systems designed to monitor both subjective perceptions and objective performance metrics. It is crucial that future implementation efforts take into account the predictors identified in this study, with particular emphasis on training quality and infrastructure adequacy, as these should serve as key performance indicators for the success of Electronic Medical Record (EMR) implementation.

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Decoding the Superorganism That Defies Death: Deinococcus radiodurans

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Abstract

Deinococcus radiodurans is one of the most radiation-resistant organisms known on Earth. Discovered accidentally in the 1950s , it has provided a unique model for studying cellular survival and repair mechanisms under extreme stress conditions. Its resistance extends beyond radiation to include desiccation and oxidative damage. The secret to its apparent "immortality" lies not in preventing damage, but in possessing a complex and efficient network for repairing DNA and protecting proteins from damage.

Keywords: *Deinococcus radiodurans; Extremophiles; Radiation resistance; DNA repair; Superorganism; Astrobiology.*

1. Introduction

If a nuclear war devastated our planet, which creature would inherit the Earth? While many might think of cockroaches, the true champion of survival is actually a microscopic bacterium - Deinococcus radiodurans (meaning "strange berry that withstands radiation"). First isolated in 1956 by Arthur W. Anderson , this extraordinary bacterium's remarkable ability to survive radiation sterilization processes intrigued the scientific community. The Guinness World Records has rightly classified this bacterium as "the most radiation-resistant lifeform in the world" , making it a subject of immense importance in understanding the limits of life itself.

2. Extraordinary Characteristics

The resilience of D. radiodurans is not based on defending its genome from initial damage, but rather on its unparalleled capacity for immediate structural and cellular repair:

1 DNA Crystalline Packing: Chromosomes are tightly arranged in a compact, ring-like helical structure . This extreme condensation prevents broken DNA fragments from dispersing after damage, keeping them in place for sequential reassembly .

2 Extended Synthesis-Dependent Strand Annealing (ESDSA): The bacterium utilizes multiple identical copies of its genome as templates for repair, employing advanced enzymatic machinery to clone small fragments and accurately stitch them back together.

3 Free Radical Elimination System: It possesses highly specialized antioxidant enzymes, including catalase and peroxidase, alongside protective carotenoid compounds that neutralize oxidative compounds .

4 Chaperone Proteins: Molecular chaperones, specifically DnaK and GroEL, actively refold radiation-damaged proteins to maintain the absolute integrity of cellular machinery.

5 Manganese Complex Accumulation: The cell accumulates extraordinarily high concentrations

of manganese ions . These ions form unique non-protein complexes that shield vital metabolic proteins from oxidation during stress .

3. Future Applications

The unique traits of D. radiodurans offer promising avenues across several fields:

Bioremediation: Engineering the bacterium to clean up highly radioactive waste sites and break down toxic organic pollutants in extreme environments .

Biotechnology: Isolating highly stable, radiation-resistant enzymes for use in demanding industrial, pharmaceutical, and chemical processes.

Medical Research: Deciphering its flawless DNA repair systems to uncover new mechanisms for cellular longevity, anti-aging therapies, and advanced cancer treatments.

4. Conclusion

Deinococcus radiodurans represents an amazing model of life's resilience . Studies have revealed that the secret to its strength lies not in preventing damage, but in possessing an immediate cellular emergency system capable of reassembling itself from the brink of death . Understanding these mechanisms represents significant progress in basic biology and opens new horizons for technological applications. In a post-apocalyptic scenario, while most life forms would perish, this incredible microorganism would likely continue to thrive, truly earning its title as the organism that defies death.

5. Recommendations

Further research should be conducted to explore the genetic and molecular mechanisms underlying the extraordinary resistance of Deinococcus radiodurans to radiation and environmental stress.

Future studies are encouraged to investigate the potential application of D. radiodurans in the bioremediation of radioactive and chemically contaminated environments.

Researchers should focus on identifying and characterizing the unique DNA repair pathways of D. radiodurans to support advances in biotechnology, medicine, and genetic engineering.

The development of industrial and pharmaceutical applications based on the bacterium’s highly stable enzymes and protective mechanisms should be further explored.

Comparative studies between D. radiodurans and other extremophilic microorganisms are recommended to better understand the limits of cellular survival under extreme conditions.

Greater attention should be given to the potential role of D. radiodurans in astrobiology and space exploration, particularly in understanding the possibility of life surviving beyondauthors also confirm that no AI tools were used for data collection, analysis, discussion, or conclusion**.**

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Molecular Mechanisms of Cellular Evasion and Granuloma Dynamics in Mycobacterium Tuberculosis Pathogenesis: A Comprehensive Review

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Abstract

Mycobacterium tuberculosis (Mtb) remains one of the most successful and lethal human pathogens in evolutionary history. Its persistence is rooted in an intricate, dual-phase lifecycle that alternates between active replication and clinical latency. Rather than remaining a passive bystander within the host immune system, Mtb actively reprograms host macrophages, subverts innate immune signaling, and exploits host tissue architecture to construct its own protective niche: the granuloma. This review provides a comprehensive analysis of the molecular mechanisms driving Mtb pathogenesis. We delineate the early stages of infection, specifically focusing on the inhibition of phagosome-lysosome fusion and the arrest of phagosomal maturation driven by bacterial effectors like PknG, PtpA, and SapM. Furthermore, we examine the Type VII secretion system (ESX-1) and its role in mediating cytosolic escape, alongside host-pathogen metabolic cross-talk where Mtb transitions to utilizing host cholesterol and fatty acids within lipid-loaded "foamy" macrophages. Finally, we analyze the structural and immunological dynamics of the tuberculous granuloma, detailing how this architecture acts as both a host defense mechanism and a bacterial sanctuary, culminating in caseation, cavitation, and transmission. Understanding these host-pathogen interactions is paramount for the development of targeted, host-directed therapeutics (HDTs) designed to overcome antibiotic resistance.

Keywords: *Mycobacterium tuberculosis, Host-Pathogen Interaction, Phagosome Maturation Arrest, ESX-1 Secretion System, Tuberculous Granuloma, Host-Directed Therapy (HDT)*

1. Introduction

Tuberculosis (TB), caused by the acid-fast bacillus Mycobacterium tuberculosis, represents a monumental challenge to global public health. Despite the availability of curative multi-drug regimens, Mtb continues to cause millions of infections annually, compounded by the alarming rise of multi-drug-resistant (MDR) and extensively drug-resistant (XDR) strains . The evolutionary success of Mtb relies entirely on its sophisticated capacity to survive, replicate, and persist within the hostile intracellular environment of the human macrophage.

When infectious droplets containing Mtb are inhaled into the alveolar spaces of a naive host, they are immediately encountered by alveolar macrophages and dendritic cells. In a standard bacterial infection, these professional phagocytes engulf the pathogen, initiating a cascade of lysosomal

fusion, vacuolar acidification, and oxidative stress that rapidly destroys the invader . However, Mtb has evolved a suite of virulence factors that dismantle this innate immune response from within.

Rather than succumbing to intracellular destruction, Mtb halts phagosomal maturation, breaches vacuolar membranes to access the nutrient-rich cytosol, and actively manipulates host transcription profiles via altered cytokine pathways . As the adaptive immune response is recruited, the host attempts to wall off the infection, creating organized cellular aggregates known as granulomas . While historically viewed as a successful host-driven containment mechanism, contemporary research demonstrates that the granuloma is a highly dynamic battleground. Mtb actively exploits this structure, utilizing it as an immunologically privileged sanctuary to enter metabolic latency, resist antimicrobial penetration, and eventually drive tissue necrosis to facilitate onward transmission .

This review explores the basic science of the host-pathogen interface in TB. By mapping the molecular pathways of cellular evasion, metabolic adaptation, and granuloma dynamics, we provide a structured overview of Mtb pathogenesis and highlight how these pathways inform the next generation of host-directed therapies.
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2.Phase I : Entry and Phagosome Maturation Arrest

The primary intracellular home of Mtb is the macrophage. Entry into the host cell is mediated by an array of pattern recognition receptors (PRRs) on the macrophage surface, including complement receptors (CR1, CR3, CR4), mannose receptors (MR), and scavenger receptors . This receptor-mediated phagocytosis internalizes the bacillus into a specialized membrane-bound vacuole termed the phagosome.

In a canonical phagocytic event, the early phagosome sequentially interacts with endocytic vesicles, migrating from an early endosome status to a late endosome, and finally fusing with a lysosome to form a highly acidic, hydrolytic phagolysosome. This maturation process is orchestrated by small Rab GTPases (such as Rab5 and Rab7) and the recruitment of the vacuolar H^+-ATPase (v-ATPase) pump, which drops the internal pH to below 5.0. Mtb completely paralyzes this maturation cascade, maintaining the phagosome at a hospitable pH of approximately 6.2–6.4 .

2.1 PknG (Protein Kinase G)

PknG is a soluble eukaryotic-like serine/threonine protein kinase secreted by Mtb within the host macrophage cytoplasm. Once inside the cytosol, PknG interrupts host intracellular trafficking. It prevents the recruitment and activation of **Rab7**, the specific GTPase required for transitioning a late phagosome into a phagolysosome (Walburger et al., 2004). By maintaining the phagosome in a permanent Rab5-positive, early endosomal state, Mtb avoids exposure to the toxic lysosomal hydrolases and proteases that would otherwise digest the bacterium.

2,2 PtpA (Protein Tyrosine Phosphatase A)

Upon internalization, Mtb secretes PtpA into the macrophage cytoplasm, where it targets two distinct host proteins to eliminate vacuolar acidification and vesicle fusion :

• **VPS33B Inhibition:** PtpA binds to and dephosphorylates the host protein VPS33B, a core component of the HOPS (homotypic fusion and vacuole protein sorting) complex. This

dephosphorylation disrupts the HOPS complex's ability to drive vesicle fusion between the late endosome and the lysosome.

- **v-ATPase Subversion:** PtpA physically binds to subunit H of the host macrophage v-ATPase proton pump. By binding directly to this machinery, PtpA blocks the pump's assembly on the phagosomal membrane, preventing the translocation of hydrogen ions (H^+) into the vacuole. Consequently, the phagosome cannot acidify, stripping the macrophage of its primary mechanism of microbial inhibition.

2.3 SapM (Secreted Acid Phosphatase M)

The recruitment of key endosomal tethering proteins, such as Early Endosome Antigen 1 (EEA1), requires the presence of a specific signaling lipid on the phagosomal membrane: phosphatidylinositol 3-phosphate (PI3P). EEA1 acts as a bridge, allowing the phagosome to dock and fuse with late endocytic compartments.

Mtb secretes SapM, a highly specialized lipid phosphatase that hydrolyzes PI3P directly from the cytosolic face of the phagosomal membrane . By depleting the phagosome of PI3P, SapM eliminates the binding sites for EEA1. Deprived of its tethering molecules, the Mtb-containing phagosome becomes structurally isolated, completely stalling the endocytic maturation pathway. The direct divergence between standard phagolysosomal routing and this arrested state is illustrated in Figure 1.

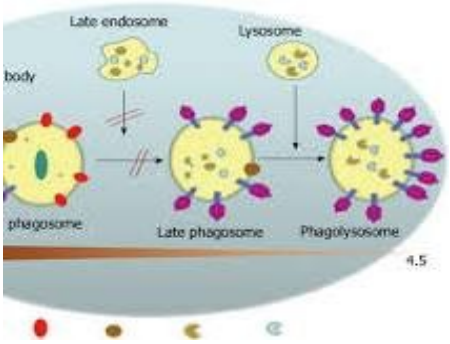

Figure 1. Molecular mechanisms of Mtb-driven phagosome maturation arrest.

Schematic comparison between canonical phagolysosome formation and the halted pathway inside an Mtb-infected macrophage. Secreted bacterial effectors PknG, PtpA, and SapM disrupt specific host trafficking elements (Rab7, HOPS, v-ATPase, and PI3P), blocking acidification and structural fusion with the host lysosome.

3. Phase II: Cytosolic Escape and Host Cell Reprogramming

While halting phagosome maturation provides a temporary refuge, remaining indefinitely inside a stagnant vacuole exposes the pathogen to eventual autophagic clearance or nutrient deprivation. To secure long-term survival, Mtb initiates a coordinated breakout into the host cell's nutrient-dense cytosol and begins actively altering host signaling networks.

3.1 The ESX-1 Type VII Secretion System

The capability of virulent Mtb strains to breach the phagosomal membrane is entirely dependent on the ESX-1 (Early Secreted Antigen Target 6 kDa secretion system 1), a complex Type VII secretion system embedded within the dense, mycolic acid-rich mycobacterial cell envelope .

ESX-1 mediates the transport and secretion of two core virulence factors: ESAT-6 (Early Secreted Antigen Target 6 kDa) and CFP-10 (Culture Filtrate Protein 10 kDa). Inside the bacterial cytoplasm, these two proteins are synthesized as a tight, helical heterodimer. Following secretion into the confined lumen of the phagosome, the acidic microenvironment triggers a structural shift, inducing the dissociation of the heterodimer .

Free ESAT-6 exhibits unique lipophilic and membrane-inserting properties. It acts as a molecular drill, inserting directly into the host phagosomal lipid bilayer and forming pore structures that destabilize membrane integrity. This localized lysis triggers a complete rupture of the phagosomal membrane, allowing Mtb to physically exit the damaged vacuole and escape into the host macrophage cytosol (Figure 2). In the cytosol, Mtb accesses rich stores of host nutrients, free amino acids, and iron, laying the groundwork for replication.

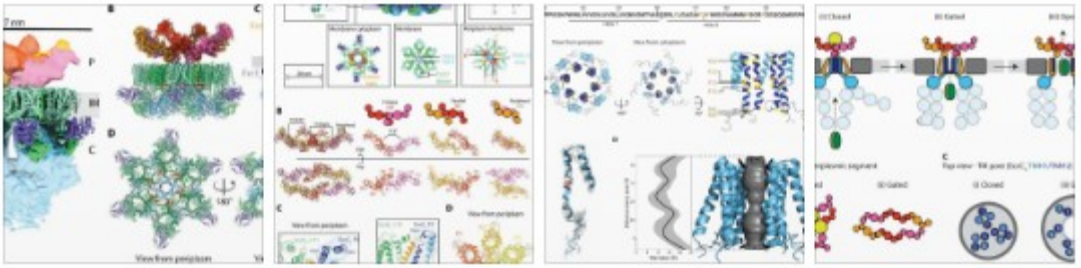

Figure 2. Structural architecture of the Type VII ESX-1 secretion machine and cytosolic escape

Close-up model of the mycobacterial cell envelope displaying the core ESX-1 complex. Secreted ESAT-6/CFP-10 heterodimers dissociate under low pH, releasing lipophilic ESAT-6 monomers that disrupt the host phagosomal bilayer to permit bacterial transition into the host nutrient-rich cytosol.

3.2 Epigenetic and miRNA Manipulation of Host Immune Signaling

Beyond physical escape, Mtb alters the host's cellular defense programs through epigenetic modifications and the induction of specific host microRNAs (miRNAs). Mtb infection triggers a highly tailored transcription program within the macrophage to suppress pro-inflammatory pathways while upregulating anti-inflammatory circuits.

•**Suppression of TNF-α via miR-125a:** Mtb selectively upregulates host miR-125a, which targets and degrades the mRNA transcripts of critical signaling adaptors in the Toll-like Receptor (TLR) pathway. This effectively blunts the production of Tumor Necrosis Factor-alpha (TNF-$\ alpha$), a cytokine vital for macrophage activation and the maintenance of granuloma structural integrity .

•**Inhibition of Autophagy via miR-17-5p:** To prevent the host cell from capturing cytosolic Mtb via selective macroautophagy (xenophagy), the pathogen drives the over-expression of miR-17-5p. This specific miRNA silences host targets like Mcl-1 and Stat3, which are essential up-stream regulators of autophagosome formation.

Additionally, Mtb releases proteins that cross into the host nucleus. For example, Rv1988 is a mycobacterial secretory protein that functions as a histone methyltransferase. Rv1988 localizes directly to the host chromosome, inducing histone H3 methylation at specific gene loci responsible

for generating reactive oxygen species (ROS). By structurally locking these host genes in an inactive heterochromatin state, Mtb dampens the macrophage's oxidative burst capacity.

3.5 Host –Pathogen Metabolic Cross-Talk :"Foamy" Macrophage

As Mtb establishes its intracellular niche, it shifts its core metabolic requirements. Instead of relying on standard carbohydrates or glycolysis for energy, Mtb shifts to a highly specialized lipid-centric diet, rewiring the host cell's lipid processing pathways to create "foamy" macrophages .

3.5 Induction of Lipid Droplet Accumulation

Mtb forces the host macrophage to accumulate massive internal stores of neutral lipids, primarily triacylglycerols (TAGs) and cholesteryl esters, giving the cells a characteristic foamy appearance under microscopic evaluation. This is achieved via two parallel bacterial strategies:

1.**Activation of PPAR-γ:** Mtb cell wall components, such as lipoarabinomannan (LAM), strongly trigger host Peroxisome Proliferator-Activated Receptor Gamma (PPAR-γ). Activation of this nuclear receptor drives the transcription of host lipid-storage proteins, specifically ADRP (Adipose Differentiation-Related Protein) and perilipin, which physically coat and stabilize intracellular lipid droplets, preventing their metabolic breakdown by host lipases .

2.**Disruption of Efflux:** Simultaneously, Mtb suppresses host cholesterol efflux transporters, such as ABCA1. This prevents the macrophage from pumping excess cholesterol out of the cell, locking the host in a permanent state of hyperlipidemia.

3.6 Bacterial Exploitation of Host Cholesterol

For Mtb, these accumulated host lipid droplets are not just storage waste; they represent a primary energy matrix and carbon source required for long-term survival and clinical latency. Mtb expresses an exceptionally large number of lipid-metabolizing enzymes within its genome, including the specialized mce4 (mammalian cell entry 4) transport system .

The Mce4 complex acts as an active, high-affinity cholesterol importer embedded in the mycobacterial membrane. Once cholesterol is brought inside the bacterial cell wall, Mtb breaks it down via its internal β-oxidation machinery, feeding the resulting carbon fragments directly into the glyoxylate shunt—an alternate metabolic pathway driven by the bacterial enzymes isocitrate lyase 1 and 2 (**Icl1** and **Icl2**) .

The glyoxylate shunt bypasses the carbon-degrading steps of the canonical tricarboxylic acid (TCA) cycle, allowing Mtb to synthesize essential carbohydrates from lipid sources without losing carbon as CO_2. This metabolic adaptation allows Mtb to sustain itself during extended periods of dormancy when glucose and oxygen are restricted.

4. Phase III :The Tuberculous Granuloma

The definitive hallmark of tuberculosis pathogenesis is the formation of the granuloma. Traditionally defined as a defensive host mechanism designed to restrict bacterial dissemination,

current molecular evidence reveals that the granuloma is a highly dynamic, highly contested structure that Mtb actively molds to serve its lifecycle requirements .

4.1 Cellular Architecture and Structural Zones

The mature tuberculous granuloma is a highly organized, spherical cellular aggregate comprising distinct immunological micro-environments. Its layout can be categorized into three distinct layers:

1. **The Necrotic Core:** Located at the literal center of the structure, this zone contains infected macrophages that have undergone necrotic cell death, mixing with extracellular bacteria, cellular debris, and a thick, lipid-rich, semi-solid matrix known as caseum.
2. **The Epithelioid and Giant Cell Ring:** Encircling the core is a dense layer of highly differentiated macrophages. Under the continuous influence of localized cytokines, these macrophages undergo structural changes:
o **Epithelioid Macrophages:** Cells that develop interlocked cell-to-cell junctions, forming a tightly sealed barrier to isolate the core.
o **Multinucleated Giant Cells (Langhans Giant Cells):** Formed via the cytokine-driven fusion of multiple macrophages, resulting in a large cell with a horseshoe-like arrangement of nuclei. These cells exhibit altered phagocytic capability.
o**Foamy Macrophages:** Packed with lipid droplets, residing primarily on the boundary of the necrotic core, feeding the extracellular bacilli .
3. **The Lymphocytic Periphery:** The outermost layer forms a fibrotic capsule laced with CD4+ and CD8+ T lymphocytes, B cells, natural killer (NK) cells, and dendritic cells. This peripheral ring provides continuous immunological oversight, tracking the core via chemical gradients. The precise concentric arrangement of these specific sub-populations is detailed in Figure 3.

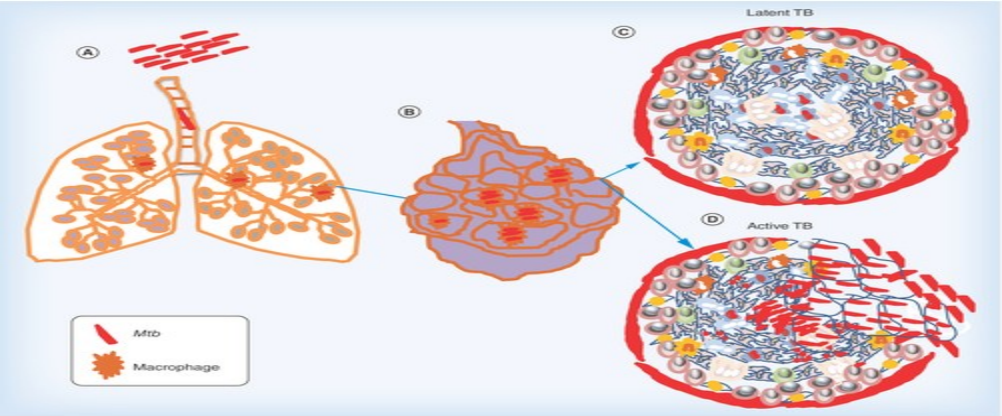

Figure 3. Concentric cellular layout and tissue microenvironments of the mature tuberculous granuloma.

A cross-sectional view of cellular organization showing the central, lipid-dense caseous core enveloped sequentially by differentiated epithelioid macrophages, Langhans giant cells, lipid-loaded foamy macrophages, and an outer lymphoid cuff bounded by a peripheral collagen capsule.

4.2 The Granuloma as a bacterial Sanctuary

While the host uses the granuloma to limit systemic bacterial spread, Mtb utilizes this precise architecture as a protective shield.

The outer fibrotic wall and dense cellular layers create an extensive physical barrier that dramatically impedes the penetration of modern antibiotics, contributing to the prolonged treatment times required for clinical eradication. Furthermore, as the center of the granuloma becomes progressively avascular, a steep oxygen gradient develops, plunging the necrotic core into profound hypoxia .

Rather than dying, Mtb senses this hypoxia via its two-component **DosR/DosS/DosT** regulatory network. The activation of the DosR regulon down-regulates standard replication machinery and turns on a latency program, shifting the bacterium into a non-replicating, metabolically dormant state. In this state, Mtb becomes highly resistant to traditional, replication-targeting antibiotics like Isoniazid, ensuring its survival for decades.

5.Comperhensive Overview of Virulence Factors

To synthesize the diverse pathways discussed, Table 1 details the major virulence factors utilized by Mycobacterium tuberculosis, their specific host targets, and their functional outcomes during infection.

Table 1. Primary Virulence Factors of *Mycobacterium tuberculosis* and Host Pathways Subverted

Virulence Factor	Bacterial Location / Secretion Mode	Primary Host Target Pathway	Biological and Pathological Outcome	Citation Reference
PknG	Secreted soluble kinase	Host Rab7 GTPase activation pathway	Blocks late endosome transformation; arrests phagosome-lysosome fusion.	Walburger et al., 2004
PtpA	Secreted soluble phosphatase	HOPS complex (VPS33B) & v-ATPase Subunit H	Prevents vacuolar membrane fusion and blocks proton accumulation, stopping acidification.	Wong et al., 2013
SapM	Secreted lipid phosphatase	Phosphatidylinositol 3-phosphate (PI3P)	Depletes membrane PI3P, preventing the recruitment of EEA1 and halting maturation.	Walburger et al., 2004
ESAT-6 /	Secreted via	Host phagosomal lipid	Induces pore formation and	Houben et

CFP-10	ESX-1 (Type VII system)	bilayer membranes	membrane lysis, driving Mtb escape into the host cytosol.	al., 2012
Rv1988	Secreted nuclear protein	Host Chromosome Histone H3	Induces epigenetic methylation, silencing genes responsible for the oxidative burst.	Stutz et al., 2022
Mce4 Complex	Outer cell wall transport system	Host intracellular cholesterol stores	Serves as a high-affinity importer, supplying carbon molecules directly to the glyoxylate shunt.	Pandey & Sassetti, 2008
Icl1 / Icl2	Intra-bacterial metabolic enzyme	Glyoxylate Shunt bypass pathway	Bypasses standard TCA cycle carbon loss, allowing survival during lipid-driven latency.	Pandey & Sassetti, 2008

6.Phase IV: Caseation, Cavitation, and Transmission

The final stage of Mtb pathogenesis represents a complete breakdown of host containment, shifting the disease from a silent, latent state to an active, infectious clinical presentation. This phase is characterized by a transition from a stable, cellular granuloma to an unstable, destructive tissue lesion .

6.1 Caseation and Liquefaction

As the structural balance inside the granuloma tips—often driven by changes in host immune status or an over-activation of localized inflammatory signals—infected macrophages undergo coordinated necrosis rather than immunologically silent apoptosis . Mtb actively drives necrosis because it breaks open the host cell without damaging the bacteria, allowing them to accumulate extracellularly.

The center of the granuloma transforms into a cheese-like, semi-solid substance termed caseum. This process, known as caseation, is accelerated by the excessive production of host Matrix Metalloproteinases (MMPs), particularly MMP-1 and MMP-9, which are secreted by surrounding neutrophils and macrophages . These enzymes degrade the structural collagen and extracellular matrix frameworks that support lung architecture.

6.2 Cavitation and Bronchial Erosion

Over time, the solid caseous core undergoes physical liquefaction. Driven by altered lipid composition and tissue hydrases, the core softens into a liquid fluid. This expanding fluid-filled

mass exerts pressure on surrounding pulmonary tissues, eventually eroding directly through the walls of adjacent bronchial airways.

Once the liquefied granuloma breaches a bronchiole, the fluid drains out, leaving behind a permanent, air-filled void within the lung parenchyma known as a pulmonary cavity. The structural breach introduces a sudden, massive influx of atmospheric oxygen (O_2) into what was previously a hypoxic core. Exposed to high oxygen levels, the dormant Mtb bacilli reactivate their aerobic respiratory pathways, initiating a phase of rapid extracellular replication. Countless millions of Mtb bacilli accumulate within the unprotected walls of the cavity.

6.3 Aerosolization and Transmission

The physical connection between the pulmonary cavity and the bronchial tree provides Mtb with a direct exit route from the host. When the patient coughs, speaks, or sneezes, the forceful expelling of air over the liquid, bacteria-rich secretions inside the cavity shears the fluid into fine aerosol droplets. Droplets smaller than 5 mm in diameter, each carrying a payload of viable, infectious Mtb bacilli, remain suspended in ambient air currents for extended periods. When these droplets are inhaled by a new, susceptible host, the entire transmission cycle begins anew .

7.Discussion and Future Therapeutic Outlook: Host- Directed Therapies (HDTs)

For over half a century, the global medical consensus for treating tuberculosis has focused exclusively on targeting the pathogen directly through complex combinations of small-molecule antibiotics. However, the rise of multi-drug resistant strains, combined with the metabolic dormancy adopted by Mtb within the granuloma, highlights the limitations of traditional antibiotic approaches.

These challenges have led to the development of Host-Directed Therapies (HDTs) . Rather than targeting the rapidly evolving bacterial genome, HDTs focus on modulating or boosting the stable genetic pathways of the human host, reinforcing the macrophage's native defense systems or modifying granuloma architecture to enhance drug delivery.

7.1 Statins As Autophagy Boosters

One of the most promising avenues of HDT research involves repurposing common cholesterol-lowering medications: HMG-CoA reductase inhibitors (statins).

As established previously, Mtb relies heavily on the accumulation of host cholesterol and lipid droplets within foamy macrophages to feed its glyoxylate shunt and maintain latency . By administering statins (such as Atorvastatin), clinicians can inhibit the host's intra-cellular mevalonate pathway, reducing cholesterol availability within the macrophage.

Beyond depriving the pathogen of its preferred nutrient source, the disruption of the mevalonate pathway triggers an integrated cellular stress response that upregulates AMPK (AMP-activated protein kinase) signaling. AMPK is a key driver of host cell autophagy. The activation of this pathway forces the macrophage to bypass the blocked phagosome maturation checkpoints, enclosing cytosolic Mtb inside autophagosomes and delivering the bacteria directly to autophagolysosomes for degradation .

7.2 Modulation of Inflammation via MMP Inhibitors

Another strategic focus of HDTs centers on protecting lung tissue from the destructive cavitation processes that drive transmission. Because tissue cavitation is driven by host Matrix Metalloproteinases (specifically MMP-1, MMP-3, and MMP-9) degrading the pulmonary matrix, utilizing targeted **MMP inhibitors** (such as Doxycycline at sub-antimicrobial doses) can preserve lung parenchyma . By stabilizing the structural matrix around the granuloma periphery, these inhibitors prevent lesion rupture and cavity formation, restricting bacterial reactivation and reducing tissue damage.

7.3 The Immunotherapy Crossroads: Lessons from Oncology

The delicate immune balance within the granuloma is highlighted by clinical observations in oncology, specifically regarding the use of immune checkpoint inhibitors (e.g., anti-PD-1 or anti-PD-L1 therapies). These cancer immunotherapies work by blocking inhibitory pathways, allowing T cells to attack malignant tumors.

However, in patients with undiagnosed latent tuberculosis, checkpoint inhibition can inadvertently cause severe, acute reactivation of TB. This occurs because sudden, uncontrolled T-cell activation disrupts the balanced, low-level inflammation required to maintain the granuloma's structural integrity. The resulting hyper-inflammatory response causes rapid caseation and necrosis of the granulomatous wall, releasing latent bacilli. This clinical cross-talk underlines the complexity of host-pathogen dynamics: therapeutic interventions must carefully balance the immune response, avoiding both immunosuppressive failure and hyper-inflammatory tissue destruction.

9. Conclusion

Mycobacterium tuberculosis is a highly adapted pathogen capable of subverting the human immune system. Its survival strategy relies on a sequence of molecular maneuvers: arresting phagosomal maturation via secreted effectors like PknG and PtpA, executing a Type VII secretion-dependent cytosolic breakout, and metabolically hijacking host lipid pathways to establish long-term residency within foamy macrophages.

The tuberculous granuloma represents the climax of this host-pathogen interaction. It stands as a complex structure where host containment and bacterial survival are deeply intertwined, ultimately leading to tissue liquefaction, pulmonary cavitation, and aerosol transmission.

Conquering tuberculosis requires looking beyond the bacterial cell wall. Future therapeutic strategies must look past standard antibiotic models and focus on the molecular cross-talk at the host-pathogen interface. By combining traditional antimicrobial agents with host-directed therapies that restore phagosomal pathways, optimize autophagy, and preserve lung tissue integrity, modern medicine can disrupt Mtb's survival strategies and pave the way toward global eradication.

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Genetic Architecture of Alzheimer's Disease: From Monogenic Determinants to Polygenic Risk

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Abstract

Alzheimer's disease (AD) represents a paradigmatic example of a complex disorder in which rare monogenic determinants coexist with a broad polygenic susceptibility background. Although highly penetrant mutations in APP, PSEN1, and PSEN2 cause early-onset Alzheimer's disease, the vast majority of cases arise from the cumulative effect of common genetic variants modulated by aging and environmental factors. This mini-review synthesizes evidence from family studies, genome-wide association studies, and next-generation sequencing to delineate the evolving genetic architecture of AD. Particular emphasis is placed on convergent biological pathways, including amyloid processing, lipid metabolism, innate immunity, and endolysosomal trafficking. Finally, unresolved heritability gaps and emerging multi-omics strategies are discussed in the context of risk stratification and precision medicine.

Keywords: *Alzheimer's disease; genetic architecture; monogenic EOAD; polygenic risk score; GWAS; APO*

1. Introduction

Alzheimer's disease (AD) is a progressive neurodegenerative disorder and the leading cause of dementia worldwide. Twin and family studies consistently estimate the heritability of AD to be between 60% and 80%, underscoring a substantial genetic contribution to disease risk. Despite this high heritability, AD does not conform to a single genetic model. Instead, it spans a continuum from rare autosomal dominant forms with near-complete penetrance to common late-onset disease driven by the additive effects of numerous low-impact variants. [1–4] This conceptual shift from a monogenic to a polygenic framework has profoundly influenced our understanding of AD pathogenesis. While early discoveries established amyloid dysregulation as a central pathogenic event, more recent studies highlight the importance of immune response, lipid homeostasis, and intracellular trafficking pathways. Understanding how these genetic components interact is essential for interpreting disease mechanisms and for developing predictive and therapeutic strategies.This review explores the basic science of the host-pathogen interface in TB. By mapping the molecular pathways of cellular evasion, metabolic adaptation, and granuloma dynamics, we provide a structured overview of Mtb pathogenesis and highlight how these pathways inform the next generation of host-directed therapies.

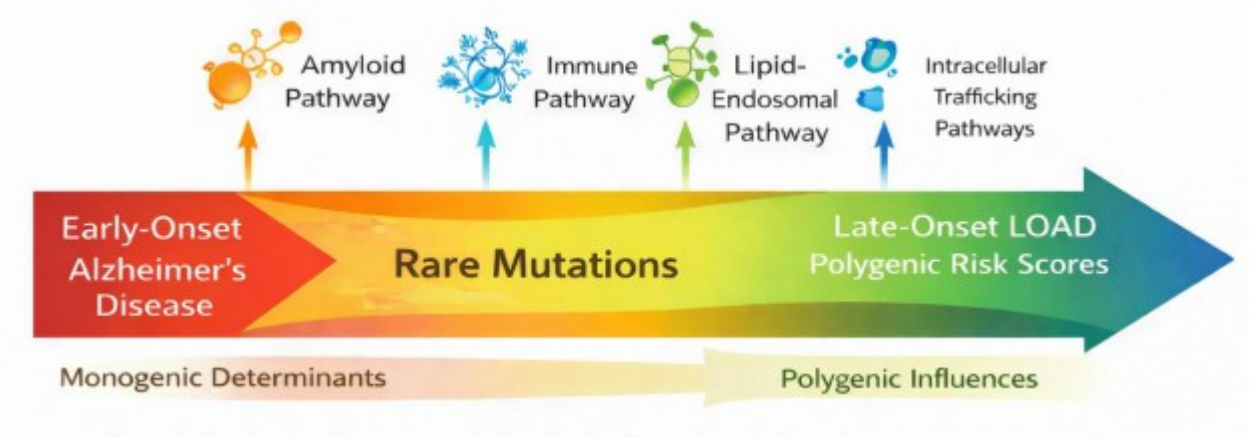

Figure 1. Genetic continuum of Alzheimer's disease.

Schematic illustration showing the spectrum from monogenic early-onset Alzheimer's disease to polygenic late-onset disease driven by cumulative genetic risk. The figure highlights convergent biological pathways including amyloid processing, lipid metabolism, immune response, and endolysosomal trafficking.

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2.Monogenic Determinants of Early-Onset Alzheimer's Disease

Early-onset Alzheimer's disease (EOAD), typically defined by symptom onset before 65 years of age, accounts for approximately 5% of all AD cases. Most familial EOAD cases are caused by pathogenic variants in APP, PSEN1, or PSEN2, which follow an autosomal dominant inheritance pattern with high penetrance. These discoveries provided the empirical foundation for the amyloid cascade hypothesis and demonstrated that altered processing of amyloid precursor protein is sufficient to trigger neurodegeneration. [3–7] Mutations in PSEN1 represent the most frequent cause of familial EOAD and are often associated with particularly early onset and aggressive clinical progression. In contrast, PSEN2 mutations are rarer and show more variable penetrance, sometimes resembling late-onset disease. Although APP mutations are uncommon, their identification was pivotal in establishing amyloid dysregulation as an initiating pathogenic event.

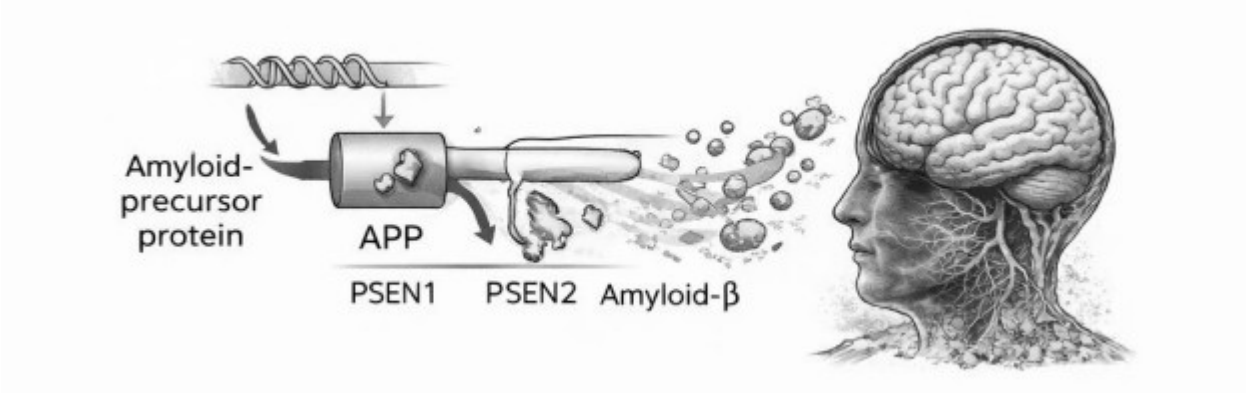

Figure 2. Schematic representation of the monogenic basis of early-onset Alzheimer's disease

Table 1. Monogenic Architecture of Early-Onset Alzheimer's Disease (EOAD)

Gene	Molecular Mechanism	Clinical Consequence
APP	Altered amyloid precursor protein cleavage	Early amyloid-β accumulation
PSEN1	Increased Aβ42/Aβ40 ratio due to γ-secretase dysfunction	Very early onset, aggressive neurodegeneration
PSEN2	Variable γ-secretase dysfunction	Later onset, incomplete penetrance

Schematic representation of the monogenic basis of early-onset Alzheimer's disease, highlighting pathogenic mutations in APP, PSEN1, and PSEN2. These mutations disrupt amyloid precursor protein processing, leading to an increased amyloid-β burden and early, aggressive neurodegeneration. Adapted conceptually from genetic studies of EOAD [3–7**].**

3 . APOE as a Genetic Bridge Between Monogenic and Polygenic Risk

The apolipoprotein E (APOE) locus constitutes the strongest genetic risk factor for late-onset Alzheimer's disease. Unlike EOAD mutations, APOE alleles modulate susceptibility rather than determine disease inevitability. Carriers of the ε4 allele exhibit a dose-dependent increase in risk and earlier age at onset, whereas the ε2 allele confers partial protection [7–9]. Mechanistically, APOE influences multiple pathogenic processes beyond lipid transport, including amyloid clearance, tau pathology, neuroinflammation, and blood–brain barrier integrity. This multifunctional role positions APOE as a biological bridge linking deterministic monogenic drivers with the broader polygenic background characteristic of late-onset disease

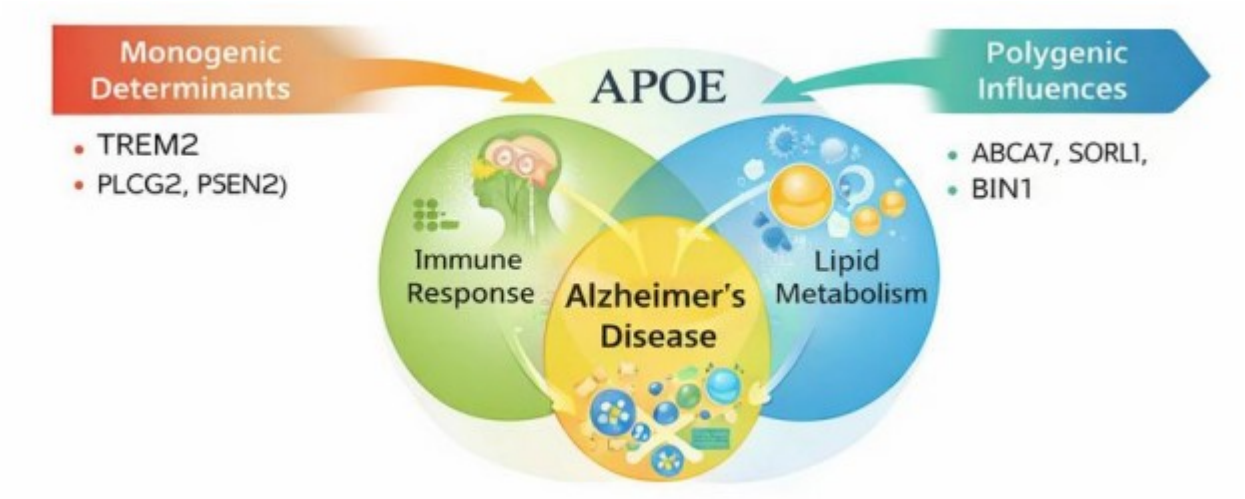

Figure 3. Polygenic risk and biological pathway convergence in Alzheimer's disease.

Overview of key pathways implicated by genome-wide association studies, including microglial activation (TREM2, CD33), lipid metabolism (APOE, ABCA7), and intracellular trafficking (BIN1,

4 . Polygenic Architecture of Late-Onset Alzheimer's Disease

Genome-wide association studies have identified dozens of loci associated with late-onset AD, revealing a highly polygenic architecture. Most risk variants individually exert modest effects but converge on shared biological pathways, particularly those related to innate immunity, lipid metabolism, and endolysosomal trafficking [10–18].

Table 2. Core Biological Pathways Implicated in Alzheimer's Diseas

Biological Pathway	Representative Genes
Amyloid processing	APP, PSEN1, PSEN2, ADAM10
Lipid metabolism	APOE, ABCA7, CLU
Immune and microglial response	TREM2, CD33, CR1
Endolysosomal trafficking	BIN1, PICALM, SORL1

Polygenic risk scores (PRS) aggregate the effects of these variants into a quantitative measure of genetic susceptibility. Recent refinements incorporating functional annotation and multi-ancestry datasets have improved predictive performance, demonstrating that substantial genetic risk exists independently of APOE status. These findings support the use of PRS as a research tool for risk stratification and for enriching clinical trial populations.

Table 3. Polygenic Architecture of Late-Onset Alzheimer's Disease (LOAD)

Feature	Description
Genetic Variants	Multiple common variants with small individual effect sizes
Risk Quantification	Polygenic Risk Scores (PRS)
Risk Modifiers	Age, vascular risk factors, lifestyle, environment
Outcome	Probabilistic disease susceptibility

5. Missing Heritability and Future Directions

Despite major advances, currently identified genetic variants explain only a portion of the estimated heritability of Alzheimer's disease. This so-called 'missing heritability' likely reflects contributions from rare variants, structural variation, gene–gene interactions, epigenetic mechanisms, and somatic mosaicism within the brain. [18–22] Future progress will depend on integrating genomic data with transcriptomic, proteomic, and metabolomic approaches, as well as expanding genetic studies to underrepresented populations. Such strategies are essential for translating genetic discoveries into precision prevention and personalized therapeutic interventions

6. Conclusion

The genetic architecture of Alzheimer's disease encompasses a continuum from rare monogenic determinants to complex polygenic risk. Although individual genetic triggers differ, they converge on a limited set of biological pathways that shape disease vulnerability and progression. A comprehensive understanding of this architecture provides a foundation for earlier risk identification and the development of more targeted therapeutic strategies. [1,2,21–25]

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Prevalence and Symptomatology of Polycystic Ovarian Syndrome in Libyan Women: A Cross-Sectional Study

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Abstract

Polycystic ovarian syndrome (PCOS) is a complicated, poorly understood hormonal condition that causes a variety of symptoms, including irregularity, which is the most common symptom, such as hyperandrogenism, metabolic abnormalities, and infertility, affecting 8 to 13% of women of reproductive age and 21% in high-risk groups. It also affects changing lifestyles and growing obesity rates throughout the world, which have contributed to an increase in PCOS occurrence. Aims: to investigate the frequency and symptoms of polycystic ovarian syndrome among Libyan women in our community. Method: A cross-sectional observational study was conducted using a structured interview technique administered via an electronic form. Over 130 participants who had a history of abnormal symptoms during their menstrual cycle in Benghazi participated in the four-month study period. The research used a pre-validated questionnaire that was adopted and modified based on the updated literature review; responses to each question were coded and entered into the Statistical Package for the Social Sciences (SPSS) version 20. Result: In this research, we discovered that the most common age group for PCOS was between 18 and 22, in contrast to the age group between 38 and 42, which was the least common, while the most common symptoms were pain (56.9%) and irregular menstruation (50%). In addition, the number of hours of sleep showed a noticeable relationship: approximately 40% of cases involved people getting less than 8 hours of sleep, which is why we recommend changing your lifestyle and losing weight. Conclusion: According to the study, there is an increase in the risk factors for chronic illnesses like PCOS, which calls for immediate action to lower their incidence and treat the underlying chronic illnesses.

Keywords: *Polycystic Ovary Syndrome; PCOS; Prevalence; Symptomatology; Libya; Cross-Sectional Study; Women's Health; Menstrual Irregularities; Lifestyle.*

1. Introduction

Polycystic ovary syndrome (PCOS), the major endocrinopathy among reproductive-aged women, affects 8 to 13% of women of reproductive age and 21% in high-risk groups. PCOS is the most prevalent reproductive disorder causing significant health consequences for women, impairing quality of life and increasing morbidity. In 2017, 1.55 million incident cases of PCOS among women of reproductive age (15-49 years) were reported globally, representing an increase of 4.47% from 2007 to 2017. The global age-standardized incidence rate of PCOS among women of reproductive age was 82.44 per 100,000 population in 2017, an increase of 1.45% from 2007 to 2017. There is no clear cause of PCOS, but exposure to lifestyle, occupational, and environmental factors may enhance or exaggerate its occurrence. Some differences in the prevalence of PCOS were reported across geographic areas; high-income countries (e.g., Europe and North America) generally showed higher rates than Asian countries. However, a lower frequency of hirsutism was

observed in studies conducted in East Asia. Differences in lifestyle habits and in the prevalence of obesity and metabolic syndrome may partially explain this variability. The cause-and-effect relationship of these aspects with PCOS remains inadequately studied, particularly regarding occupational and lifestyle exposures. The hallmark features of PCOS include anovulation, hyperandrogenism, and polycystic ovaries. Other major manifestations include luteinizing hormone hypersecretion, metabolic disturbances, hyperinsulinemia, insulin resistance, glucose intolerance, dyslipidemia, hirsutism, acne, obesity, type II diabetes mellitus, and infertility. There is also increasing evidence that women with PCOS are more likely to suffer from mood disorders; the underlying mechanisms remain unclear, though obesity, insulin resistance, elevated androgens, and distress related to hirsutism, weight gain, acne, and infertility are contributing factors. If left untreated, PCOS can worsen fertility and obstetric outcomes and increase cardiovascular, metabolic, and oncological risks, as well as psychological disorders such as stress and depression. Unfortunately there is no cure for PCOS, but treatments can improve symptoms. Management combines lifestyle alteration with medical management: a healthy, balanced diet and regular exercise to prevent excessive weight gain and reduce PCOS-related complications; metformin to improve insulin resistance; combined oral contraceptives for menstrual cycle regulation and hyperandrogenism; and, when needed, anti-androgens for refractory hyperandrogenism. For infertility due to PCOS, management includes lifestyle changes, medicines, or surgery to stimulate regular ovulation, and in vitro fertilization (IVF) may be used.

2. Method

This section describes the study setting and design for assessing the prevalence and symptoms of polycystic ovary syndrome. The study was conducted on a sample of the Libyan population who had a history of abnormal symptoms during their menstrual cycle.

Description of the research setting

A cross-sectional observational study was conducted in Benghazi between 19th January and 19th April 2024. Participants were asked to consent to participate in the study verbally and were interviewed using a pre-validated questionnaire, which took 5 to 7 minutes to complete.

Study design

Quantitative research was conducted using a structured interview methodology. A total of 130 questionnaires were recorded using an electronic technique. The advantages of this approach include the ability to provide clarifications, a better response rate, the possibility of exploring the problem in depth, gaining participant confidence, and the opportunity for further investigation. Participants were informed that the researchers were university students in the Faculty of Pharmacy at the Libyan International Medical University.

Selection and exclusion criteria

Inclusion criteria: Participants allowed to take part were Libyans, aged 18 to 42 years, with a history of symptoms during their menstrual cycle.

Exclusion criteria: Participants excluded from this study were those aged under 18 or over 42 years, who had no recurrent symptoms during the cycle, or who were of a different nationality.

Research tool

The questionnaire was piloted using a snowball sampling technique with 5% (n=8) of the target sample. Following piloting, further modifications were made to enhance its comprehensiveness based on various literature reviews. Data from the pilot test were excluded from the final analysis. The final questionnaire consisted of 16 closed-ended questions, distributed across Part A and Part B.

Part A: Demographic data (such as age, height, weight).

Part B: Daily activity, lifestyle, and information about the menstrual period.

Ethical consideration

The researchers obtained written permission from the research center to apply the questionnaire.

Statistical Analysis

Responses to each question were coded and analyzed using the Statistical Package for Social Sciences (SPSS) version 20 for Windows (SPSS Inc., Chicago, Illinois). The analysis included frequencies of discrete variables.

3. Results

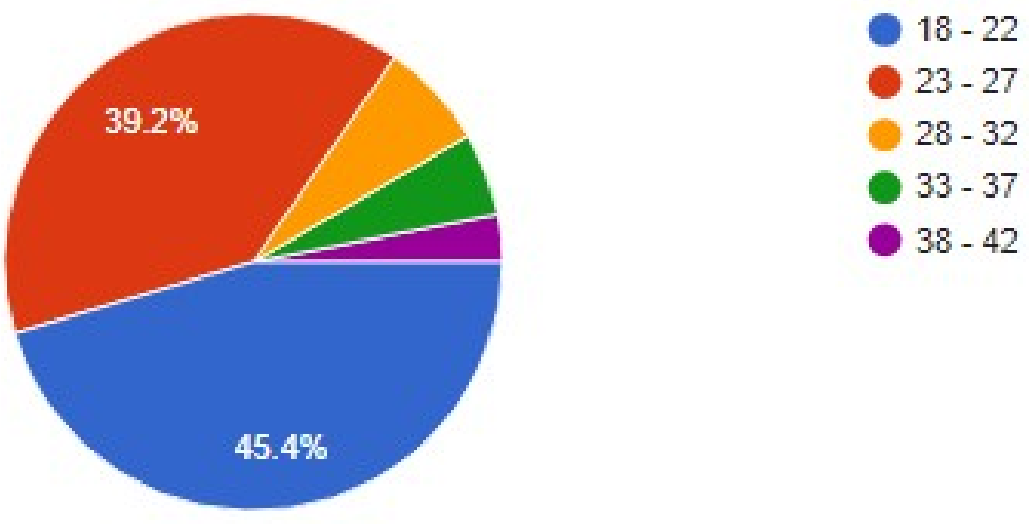

Figure 1. Age distribution.

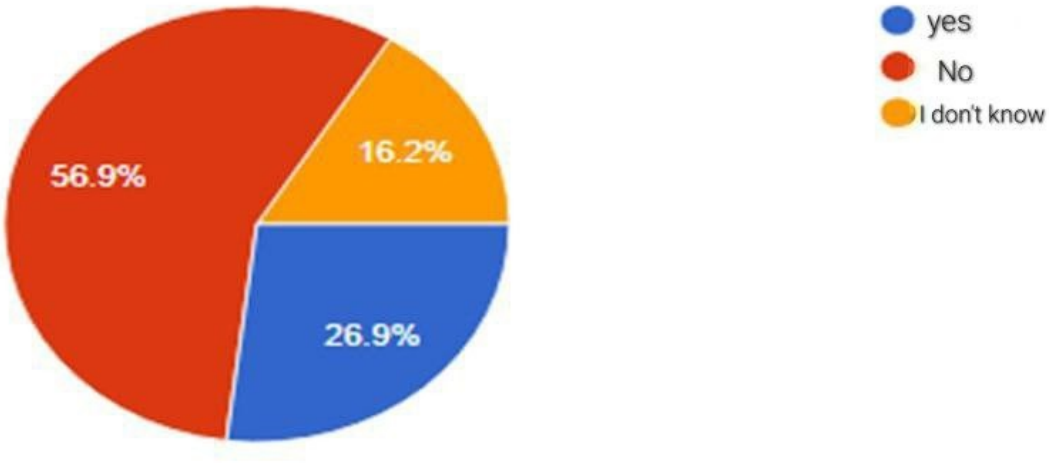

Figure 2. Are you affected by this disease?

Table 1. The symptoms considered with this disease.

Symptoms	Percentage of each symptom
Weight gain	(38.5%) 50
Irregular menstrual cycle	(50%) 65
Excessive hair growth around the face, abdomen, and back	(31.5%) 42
Thinning hair	(24.2%) 34
Acne	(44.6%) 58
Absence of menstrual cycle	(24.6%) 32
Infertility	(3.8%) 5
Ovarian cysts diagnosed by ultrasound	(16.2%) 21
Hormonal disorders detected by blood test	(14.6%) 19
Painful menstrual cycle	(56.9%) 74
Bleeding between menstrual cycles	(8.5%) 11
Diabetes/insulin resistance	(7.7%) 10
Total (n=120)	Total percentage (100%)

Table 2. The line of treatment followed by the participants' doctors.

Treatment	Percentage of use of each treatment
Description of oral contraceptives	(26.8%) 15
Description of forms of contraception	(5.4%) 3
Description of metformin, a drug that lowers blood sugar	(16.1%) 9
Description of clomiphene or other drugs that stimulate ovulation	(8.9%) 5
Description of statins, which are drugs that lower cholesterol	(3.6%) 2
Description of other drugs	(33.9%) 19
Surgery	(12.5%) 7
Advice to change lifestyle, i.e., lose weight, follow a	(35.7%) 20

diet, and exercise

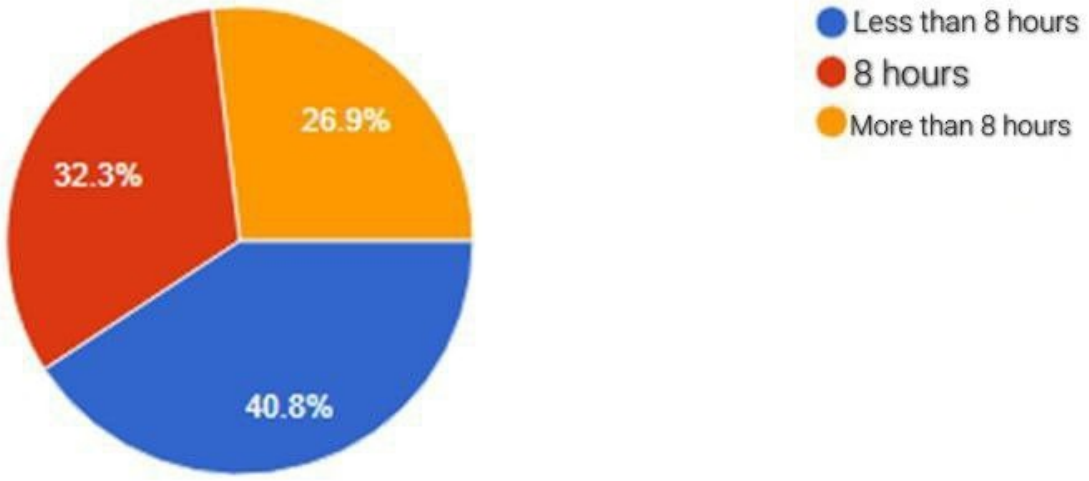

Figure 3. Average sleeping hours at night.

4. Discussion

When we studied PCOS in 130 participants, we found that it was most diffuse between the ages of 18 and 22, accounting for 45.5% of cases. While the cause of polycystic ovaries is unknown, changes in hormones during adulthood appear to play a significant role. PCOS is linked to multiple reproductive and psychological complications that are of serious concern in a patient's life; however, in population-based research including individuals participating in a health plan in Northern California, 0.81% of teenagers aged 15 to 19 had been diagnosed with PCOS. The prevalence of PCOS, regardless of diagnosis, was found to be 3% in an Iranian study that examined schoolgirls based on a questionnaire assessing PCOS symptoms.

As a result, when we conducted our study on the diagnosis of polycystic ovary syndrome (PCOS), the results showed that a large percentage of people, up to 59.9%, were not diagnosed with the disease. This is likely due to national culture, particularly since many women experience symptoms but are not diagnosed. For this reason, raising awareness and obtaining an accurate diagnosis are the first steps in managing PCOS, as they improve the patient's quality of life.

According to our results, most participants were not diagnosed with the syndrome despite having symptoms; a large percentage answered “I don't know” (66%), and the second largest percentage (4.5%) were participants aged 20 years, which further explains why the majority of affected participants in this research were aged 18-22. This underscores the importance of awareness of PCOS and the need for early diagnosis so that patients can avoid its serious complications.

Since the purpose of this research was to identify the symptoms of PCOS, this was one of the questionnaire questions. Among the 130 patients who answered, the most common symptom was pain during the menstrual cycle (dysmenorrhea), reported at 56%, likely due to increased levels of

prostaglandins, which cause increased contractions of the myometrium and uterine blood vessels, producing a relative uterine ischemic state. This is consistent with the finding that the second most common symptom in the current study was menstrual irregularity, at 50%. In contrast, a study by fourth-year medical students in Tripoli, Libya, found that among 21 patients with PCOS, the most common symptom was menstrual irregularity, at a rate of 9.5% .

The high incidence of polycystic ovary syndrome has become an international health concern due to the serious complications that can occur if the syndrome is left untreated, such as infertility. Fortunately, there are many treatment options, which were addressed in the questionnaire. The most recommended treatment by specialist doctors was lifestyle change. Although the exact cause of PCOS is unknown, obesity affects 50% of patients with the syndrome. Insulin resistance is found in many women with PCOS even if they are not overweight; Huber-Buchholz et al. found that reducing central fat and improving insulin sensitivity through lifestyle changes leads to normal ovulation in women with PCOS, even without significant weight loss.

Although the cause of PCOS is unknown, some factors may contribute to its development. When asked “Are you exposed to a lot of stress?”, 50% of participants answered “often.” Another study found that stress plays an important role in the development of PCOS, and additional studies should consider evaluating and managing stress in PCOS as it may be relevant to understanding its pathogenesis.

When asked “Do you follow a healthy eating system?”, more than 50% of participants answered “never.” Some studies found that frequent consumption of fast food was associated with a 1.7 times greater risk of developing PCOS, likely because fast food is typically high in saturated fat; irregular eating habits lead to fluctuations in glucose levels, insulin resistance, and increased hormonal imbalance such as hyperandrogenism, increasing the risk of developing PCOS.

Overall, 40.8% of participants reported sleeping less than 8 hours, and more than 40% reported not having a fixed sleep schedule, indicating a relationship between sleep schedule and PCOS. Sleep is a beneficial factor in lifestyle that is necessary for women's well-being; women with PCOS have been shown to have more diverse sleep disturbance symptoms (16.14%, 402/2,491).

5. Conclusion

The current study shows that the prevalence of many risk factors for chronic diseases, such as PCOS, is increasing and urgently requires interventions to reduce their prevalence and address the chronic diseases they contribute to.

6. Limitation of the Study

This study was conducted on a relatively small sample of people, but it provides useful information regarding the risk factors in the community setting. The findings need to be interpreted within the context of the following potential limitations:

1. The quality of non-responders was not evaluated; thus, the true dispensing patterns of drugs may deviate to some extent from the current results.

2. Recent statistical information about Benghazi was not available.
3. A sound comparison of our data with other reports was difficult because of differing age groups, methodologies, drug classifications, and health systems.
4. Since this study was conducted in one city with a relatively small sample size, it is difficult to generalize the data to the whole Libyan population.
5. Poor internet access, combined with a short research period.
6. Subjects were randomly approached, implying some lack of rigor in the recruitment method.

7. Recommendation

We hope the following recommendations will receive due consideration:

1. Strengthen political commitment to non-communicable disease (NCD) prevention at all levels of government.
2. Integrate the delivery of basic health care for NCD prevention and management into primary health care systems.
3. Expand the package of essential NCD-related interventions available at the primary healthcare level, including a prioritized and realistic set of high-impact, cost-effective interventions to detect and treat common conditions.
4. Address health system gaps by strengthening surveillance systems, the capacity of the health workforce, and access to essential medicines and technology.
5. Remove financial barriers to essential health-care interventions, such as user fees, and reduce out-of-pocket payments.
6. Increase health promotion activities targeting schools, institutions, and workplaces, advocating a healthy lifestyle and educating the public on the harmful effects of smoking, secondhand smoke, excessive alcohol consumption, excess fat and salt intake, and lack of physical activity.
7. Strengthen physical education programs in schools from kindergarten to the tertiary level.
8. Implement recommendations from expert consultation reports, such as the WHO/FAO recommendations on diet, nutrition, and prevention of chronic diseases.
9. Set population nutrient goals and recommend a minimum intake of 400 g of fruits and vegetables per day for the prevention of chronic diseases such as heart disease, cancer, diabetes, and obesity.

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The Multisystem Pathophysiology of Post-COVID-19 Syndrome: A Contemporary Summary of Clinical Knowledge

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Abstract

Now viewed as a public health and economic challenge rather than a peculiar post-viral issue, post-COVID-19 syndrome (PCS) — colloquially referred to as "Long COVID" — is estimated to impact 10-15% of people following initial infection . PCS is a heterogeneous, multi-organ illness characterized by persistent, relapsing, or newly occurring symptoms at or beyond two months after infection, in the absence of an alternative diagnosis [1]. This is a narrative review which synthesizes emerging clinical evidence for the integrated pathophysiological mechanisms of PCS, namely: incomplete viral clearance, persisting immune dysregulation, microvascular injury to the endothelium, hypercoagulability, and autonomic dysregulation. We then present these underlying drivers and correlate them with systemic, neurological, cardiovascular, and pulmonary findings, and finish with a consideration of progressive, personalized treatment regimens.

Keywords: *Post-COVID-19 Syndrome; Long COVID; Pathophysiology; Viral Persistence; Neuroinflammation; Microclots; Dysautonomia; Endothelial Dysfunction.*

1. Introduction

The emergence of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) brought about an acute public health crisis and an immediate medical response unlike any other previously experienced globally. However, recovery from the initial phase of Coronavirus Disease 2019 (COVID-19) is often incomplete and protracted. Post-COVID-19 Syndrome (PCS), an official diagnosis by the WHO defined as the continuation or new development of symptoms lasting beyond three months after infection and at least two months from the start of symptom onset , and colloquially referred to as "Long COVID," represents a post-viral crisis that may be affecting over 400 million people globally and poses a major burden on health and economic infrastructure . PCS is a multisystem condition and occurs across a variety of organ systems. Most strikingly, the occurrence of PCS appears unrelated to acute infection severity and is commonly observed following either mild or asymptomatic infection . This article is a narrative review that presents a contemporary summary of the mechanisms contributing to PCS and its multisystem presentation, along with future therapeutic considerations.

2. Materials and Methods

This study is organized as a narrative review that summarizes new research on Post-COVID-19 Syndrome and current clinical knowledge. To gather peer-reviewed research, clinical trials, and neuroimaging/post-mortem data about the long-term consequences of SARS-CoV-2, a thorough review of the literature was conducted. The literature synthesis was limited to papers that examined systemic clinical manifestations and underlying biochemical abnormalities. To demonstrate

mechanistic linkages, collected data were matched against organ-specific domains (neurological, cardiovascular, pulmonary, and endocrine) and classified into fundamental pathophysiological drivers (e.g., viral reservoirs, immunological cascades, and microvascular disease). Clinical consensus indicates that PCS is not a single, isolated medical entity, but rather a multi-organ illness triggered and sustained by a constellation of overlapping biological mechanisms.

3. Results and Discussion

3.1 Core Pathophysiological Drivers

It has been largely accepted within the clinical community that PCS is not one single entity, but rather a multi-organ illness triggered and sustained by a constellation of overlapping biological mechanisms . A generalized cascade from initial viral exposure through multisystem manifestations is shown in Figure 1.

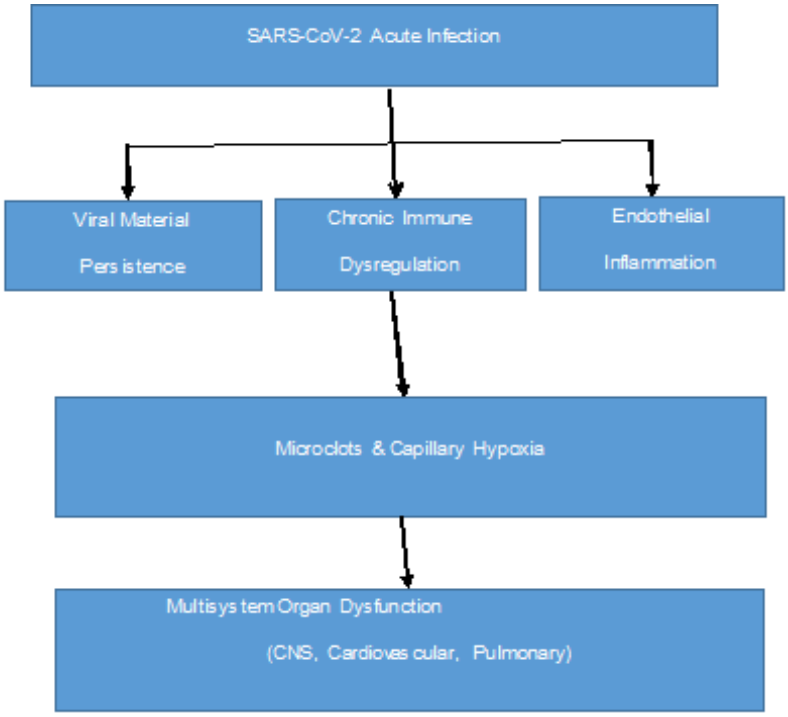

Figure 1. Schematic flow diagram demonstrating the interconnected pathways of cellular and tissue stress leading from acute SARS-CoV-2 infection to microclotting and chronic multi-system organ dysfunction.

The loss of incomplete viral clearance and viral reservoir

The longevity of highly glycosylated SARS-CoV-2 spike protein persistence in the body explains chronicity. Often, this persistently lodged structural protein binds pattern recognition receptors (PRRs) on innate immune cells, such as the non-classical CD14+ and CD16+ monocytes. Long after the acute phase has subsided, the PRR binding initiates prolonged intracellular pro-inflammatory signaling . This can lead to localized tissue injury and downstream vascular dysfunction, as shown in Figure 2.

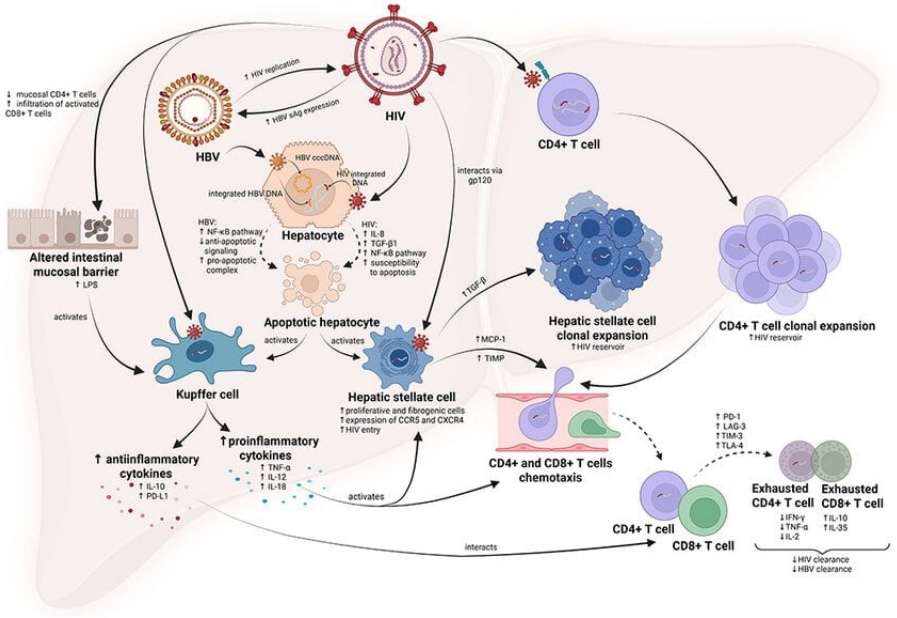

Figure 2. Viral antigen persistence mechanism. The diagram shows retained structural spike proteins that repeatedly bind pattern recognition receptors (PRRs) on non-classical (CD14+, CD16+) monocytes.

Immune Dysregulation and Autoimmunity

Persistent exposure to viral antigens brings about deep systemic immunological changes at both innate and adaptive cellular levels. In PCS, one finds constant activation of microglia, T-cell exhaustion, and high levels of systemic pro-inflammatory cytokines such as IL-6, IL-1 beta, and TNF-alpha . The increased systemic inflammation also primes for hypersensitivity and molecular mimicry. This may result in functional autoantibodies against receptors and vascular structures, leading to widespread organ damage and autonomic dysfunction.

Microvascular Pathology and Hypercoagulability

The blood vessel endothelium is dense in Angiotensin-Converting Enzyme 2 (ACE2) receptors and, consequently, becomes an important target for SARS-CoV-2. Persistent inflammation within the endothelium alters the equilibrium between the coagulation-fibrinolysis cascade and leads to the formation of functionally abnormal, fibrinogen-derived microclots that are not susceptible to normal fibrinolysis , as shown in Figure 3. Together with persistent endothelial dysfunction and increased von Willebrand factor levels, these microclots impede capillaries, leading to partial microcapillary obstruction, generalized tissue hypoperfusion, and systemic ischemia, which has been associated with global fatigue and exercise intolerance.

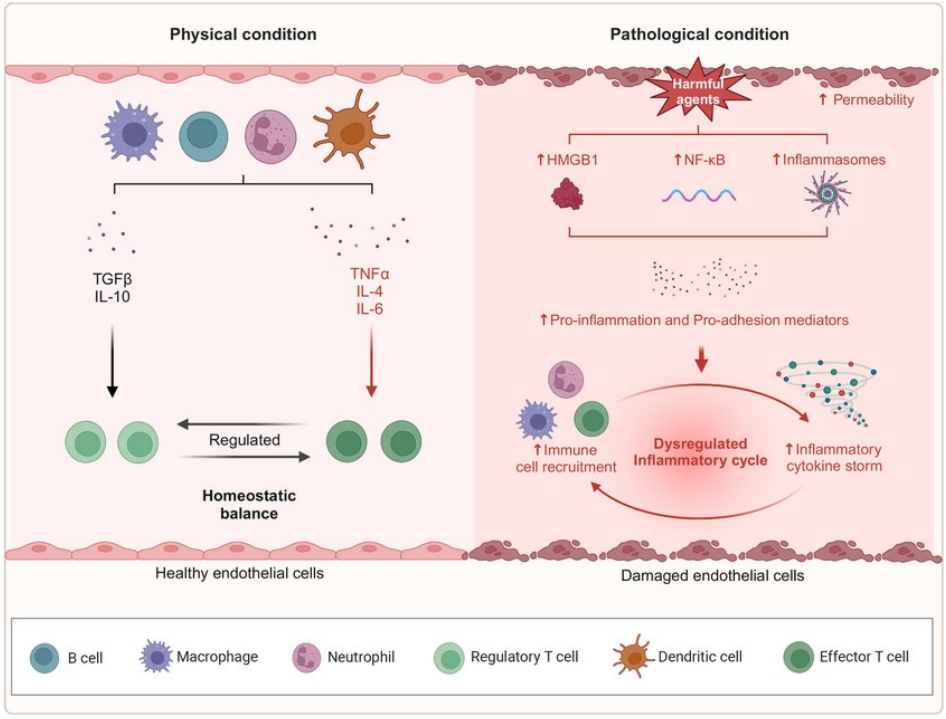

Figure 3. Endothelial inflammation and microclot formation. Chronic endothelial inflammation impacts the coagulation pathway. The blood is rendered hypercoagulable, and microclots form which are resistant to normal fibrinolysis. Obstruction of capillaries leads to restricted oxygen flow and tissue ischemia.

3.2 Organ-Specific Manifestations

These pathophysiological processes lead directly to specific manifestations across multiple physiological domains, summarized in Table 1.

Table 1. Organ-Specific Clinical Presentations and Linked Pathophysiological Mechanisms.

Physiological Domain	Predominant Clinical Symptoms	Primary Pathophysiological Drivers
Neurological / Psychiatric	Cognitive impairment (“brain fog”), executive dysfunction, profound .fatigue, sleep disturbances	Neuroinflammation, microglial over-activation, blood-brain barrier compromise, and cerebral microvascular .thrombosis
Cardiovascular	Chest pain, palpitations, exercise intolerance, orthostatic intolerance / Postural Orthostatic Tachycardia .Syndrome (POTS)	Myocardial microvascular ischemia, autoantibody engagement with GPCRs, autonomic neuropathy, and .localized perivascular fibrosis
Pulmonary	Persistent dyspnea, chronic cough, reduced gas exchange capacity .(DLCO)	Airway epithelial damage, localized air trapping, lung perfusion abnormalities, and .diffuse alveolar thickening
Endocrine / Systemic	Post-Exertional Malaise (PEM), adrenal insufficiency, circadian .rhythm disruptions	Cytokine-induced disruption of the hypothalamic-pituitary-adrenal (HPA) axis and mitochondrial/immunometabolic

.failure

Neurological Syndromes

"Brain fog" affects more than 60% of long-term sufferers. Reduced gray matter thickness, cerebral micro-hemorrhages, and increased neuroinflammatory markers are shown by neuroimaging and post-mortem examinations. Chronic cognition and memory problems are caused by elevated systemic cytokines (such as CCL11) that pass through a deficient blood-brain barrier, disturbing the neural stem cell milieu and hindering neurogenesis.

Cardiovascular and Autonomic Strain

POTS and other forms of dysautonomia are very common. Chronic inflammation and endothelial damage interfere with the autonomic nervous system's ability to control the vasculature. Unchecked venous pooling brought on by orthostatic stress causes compensatory tachycardia, lightheadedness, palpitations, and chest pain.

3.3 Evolving Therapeutic Paradigms

Since there is not a single diagnostic marker for PCS, existing management approaches are individualized and symptom-based, managed by a multi-disciplinary team.

1. Activity pacing and energy conservation

High levels of physiotherapy, which would lead to increased neuro-inflammation and a push-crash cycle for patients who suffer from post-exertional malaise (PEM), must be avoided. Rather than utilizing a typical exercise regimen, the best advice would be a strict activity pacing routine.

2. Pharmacological modulation of neuro-inflammation

A successful off-label approach that has been utilized in clinical settings with a promising response in managing microglia and modulating CNS inflammation is low-dose naltrexone (LDN).

3. Immune and histaminergic blockage

Administration of H1 and H2 antagonists and mast-cell stabilizers is beneficial for reducing symptoms related to type-1 hypersensitivity reactions and MCAS.

4. Vascular and coagulation support

Due to microclots and overall hypercoagulability of the body, medications targeting blood coagulation-fibrinolysis pathways (natural fibrinolytic agents such as nattokinase) and systemic anti-inflammatories (colchicine) are in a trial phase for widespread clinical use to promote blood flow.

4. Conclusion

PCS is a complex, multiorgan disorder caused by viral persistence, chronic inflammation, and endothelial microvascular disease. Understanding the interplay between these processes in the

development of systemic tissue hypoxia and autonomic dysfunction is crucial for guiding the development of appropriate clinical solutions. Prioritizing cohesive, mechanism-driven treatment plans over isolated organ-focused protocols is paramount. The landscape of clinical management must continue to evolve through extensive, multisite randomized controlled trials in the pursuit of cures rather than just symptom palliation.

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Prevalence and Patterns of Musculoskeletal Disorders Among Doctors Working in Invasive Procedures in Benghazi Medical Center, 2018

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Abstract

Background: Musculoskeletal disorders (MSDs) are a leading occupational health concern among healthcare professionals. Doctors performing invasive procedures face significant risk due to prolonged static postures and repetitive motions.

Objective: To evaluate the prevalence, patterns, and associated factors of MSDs among doctors in invasive specialties at Benghazi Medical Center.

Methods: A cross-sectional study was conducted in 2018 involving 200 doctors across ten specialties. The Nordic Musculoskeletal Questionnaire (NMQ) assessed pain and functional limitations in various body regions over the past 12 months and 7 days. Statistical analysis included descriptive measures, chi-square tests, and logistic regression using SPSS v25.

Results: Of the 200 participants, 62% were female, with a mean age of 39.4 years. The overall prevalence of MSDs was 86.5%, with lower back pain (59.5%) being the most reported, followed by shoulder (29%) and knee pain (28%). Gender differences were noted, with females experiencing higher rates of hip/thigh and shoulder issues. Specialty-specific risks showed ENT surgeons significantly affected by neck and wrist/hand pain.

Conclusion: MSDs are prevalent among doctors performing invasive procedures. Preventive strategies, including ergonomic training and workplace modifications, are recommended to mitigate these occupational hazards.

1. Introduction

Background: Musculoskeletal disorders (MSDs) are injuries affecting muscles, tendons, ligaments, nerves, and other components of the musculoskeletal system. MSDs arise from occupational exposures, including repetitive motions, awkward postures, and sustained physical activity. Healthcare professionals, especially those in surgical or invasive fields, face heightened risks due to the physical demands of their work.

Objective: This study aims to assess the prevalence and patterns of MSDs among doctors at Benghazi Medical Center, focusing on specialty-specific risk factors and gender differences.

2. Methods

Study Design and Setting

A cross-sectional survey was conducted at Benghazi Medical Center among doctors in ten invasive specialties between June and December 2018.

Participants

Inclusion criteria included Libyan doctors with a minimum of one year of specialty experience, regularly performing procedures lasting over 30 minutes. Non-Libyan doctors, those with less than one year of experience, or individuals unavailable during the study period were excluded.

Sampling and Sample Size

Convenience sampling was employed, with a total of 200 participants from specialties such as gynecology, general surgery, and neurosurgery.

Data Collection Tools

The Nordic Musculoskeletal Questionnaire (NMQ) was used to gather data on MSD prevalence, pain severity, and functional limitations in 12 body regions.

Data Analysis

Descriptive statistics summarized demographics and prevalence rates. Associations between variables were analyzed using chi-square tests and logistic regression. Significance was set at $p \leq 0.05$.

3. Results

Demographics

- Gender: 38% male, 62% female.
- Age: Mean 39.4 ± 8.4 years, range 27-63 years.
- Specialty distribution: Gynecology (46%), general surgery (18%), ENT (10%).

Prevalence of MSDs

- Overall prevalence: 86.5%.
- Commonly affected regions: Lower back (59.5%), shoulders (29%), knees (28%), and neck (24.5%).

Risk Factors

- Gender: Females experienced higher rates of hip/thigh and shoulder pain ($p < 0.05$).
- Specialty: ENT surgeons were significantly affected by neck and wrist/hand pain ($p < 0.05$).
- BMI: 38% of participants were overweight, and 28% were obese, correlating with higher MSD rates.

Severity of Pain

- Mild pain: 42.5%.
- Moderate pain: 41%.
- Severe pain: 16.5%.

4. Discussion

Comparison with Literature: The prevalence of MSDs in this study aligns with global findings, which report high rates of lower back and shoulder pain among surgeons and other specialists. Similar patterns have been observed in studies from Saudi Arabia and Canada, highlighting occupational ergonomics as a critical factor.

Gender and Specialty Trends: Females exhibited higher susceptibility to certain MSDs, potentially due to anatomical and hormonal differences. ENT and gynecology specialists reported significant neck and upper limb pain, likely due to prolonged static postures and intricate hand movements.

Implications for Practice: The findings underscore the urgent need for ergonomic interventions, such as adjustable surgical tables, anti-fatigue mats, and training in proper posture.

Limitations: The study's cross-sectional nature limits causal inferences. The convenience sampling method may introduce selection bias.

5. Conclusion

Musculoskeletal disorders are a prevalent occupational hazard among doctors in invasive specialties at Benghazi Medical Center. Targeted ergonomic interventions and preventive strategies are essential to improve occupational health and patient care quality.

6. Recommendations

1. Implement ergonomic training programs for healthcare professionals.
2. Conduct longitudinal studies to evaluate the effectiveness of interventions.
3. Integrate ergonomic assessments into workplace safety protocols.

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