Journal Homepage: www.ijarpr.com ISSN: 3049-0103 (Online)

International Journal of Advance Research Publication and Reviews

Vol 02, Issue 08, pp 570-592, August 2025

Pathogenesis of Silent or Hidden Metastasis in Infrequent Organs: A Systematic Review of Cardiac and Pancreatic Involvement with Global and Nigerian Perspectives

Ebenezer Amarachukwu Okoh[1*], Chimezie Williams Madu[2] and Daniel Onyedikachi Okeke[3]

[1]Department of Pathology and Laboratory Medicine, Delta State University, Teaching Hospital, Oghara Nigeria
[2]Bradford Teaching Hospitals NHS Foundation Trust.
[3]Primary Health Care, Bradford Teaching Hospitals NHS Foundation Trust.
Email - danielokeke201@gmail.com
DOI : https://doi.org/10.55248/gengpi.6.0825.3069

ABSTRACT

Silent or hidden metastases represent a critical yet underexplored challenge in oncology, where secondary tumors develop in organs that are infrequently affected and often escape clinical detection. The heart and pancreas, despite their essential physiological roles, rarely serve as metastatic sites, yet their involvement portends poor prognosis when present. This systematic review synthesizes current global and Nigerian evidence on the pathogenesis, histopathological markers, and clinical outcomes of cardiac and pancreatic metastases. Following the PRISMA 2020 guidelines and with protocol registration in PROSPERO (CRD42025142345), a comprehensive search of PubMed, Scopus, Web of Science, and Embase was conducted for studies published between 2015 and 2025. Of 1,246 articles retrieved, 45 met inclusion criteria, emphasizing histopathological confirmation and human clinical relevance. Globally, cardiac metastases were most frequently linked to lung (38%), breast (21%), and melanoma (11%) primaries, while pancreatic metastases predominantly originated from renal cell carcinoma (60%), followed by lung and breast cancers. Key immunohistochemical markers, including CK7, CK20, CDX2, S100, and PAX8, facilitated tumor origin identification and guided diagnostic precision. Nigerian studies highlighted systemic underdiagnosis, with most cases detected incidentally during autopsies, reflecting diagnostic limitations within resource-constrained healthcare environments. The review underscores that the pathogenesis of silent metastases is multifactorial, involving hematogenous spread, lymphatic dissemination, and microenvironmental adaptation within the host organ. Early recognition requires robust integration of imaging modalities with histopathological tools, which remain the cornerstone of definitive diagnosis. Improving diagnostic capacity in low-resource settings is imperative to reduce delayed recognition and optimize therapeutic interventions, ultimately improving survival outcomes for patients with these elusive metastatic presentations.

Keywords: Silent metastasis, Cardiac metastasis, Pancreatic metastasis, Histopathology, Immunohistochemistry, Nigeria

1. INTRODUCTION

1.1 Contextual background on metastasis and its clinical burden

Metastasis remains the most lethal hallmark of cancer, responsible for over 90% of cancer-related deaths worldwide [1]. It is a multistep biological process in which cancer cells detach from the primary tumor, invade surrounding tissue, enter the circulatory or lymphatic system, and colonize distant organs [2]. The clinical burden is magnified by the fact that metastatic disease is frequently resistant to conventional therapies, thereby limiting long-term survival even in settings with advanced oncologic care.

In global cancer statistics, the incidence of metastatic spread is strikingly high. For example, liver and lung metastases are frequent across many primary tumor types, while brain and bone involvement carry especially poor prognostic implications [3]. Patients presenting with advanced metastatic disease often experience profound deterioration in quality of life due to pain, cachexia, organ failure, and systemic immune dysregulation. This constellation of complications increases healthcare costs exponentially, demanding not only expensive therapeutic regimens but also prolonged hospitalization and palliative services.

Despite notable therapeutic advances including targeted therapy and immunotherapy the metastatic cascade continues to evade complete control [4]. This reality underscores metastasis as not merely a biological event but a pressing clinical challenge of global dimension. Sub-Saharan Africa, and Nigeria in particular, confronts the dual challenge of rising cancer incidence and inadequate specialized oncology centers, resulting in delayed diagnosis and limited treatment access.

The global burden is captured not only in mortality rates but also in socioeconomic losses tied to lost productivity and caregiver strain [5]. Effective strategies for early detection and intervention at the metastatic stage are therefore critical. Figure 1 illustrates the conceptual framework of the metastatic cascade, while Table 1 provides a comparative overview of high-burden metastatic sites and their associated prognostic outcomes.

1.2 Importance of hidden/silent metastasis in infrequent organs

While most clinical focus has centered on common metastatic destinations such as the liver, lung, and brain, silent or hidden metastases in less frequent organs present a particularly insidious challenge [6]. These metastases often remain undetected until autopsy or advanced imaging is performed late in the disease course. Examples include metastasis to the spleen, thyroid, adrenal glands, and even the pancreas sites not traditionally prioritized in staging protocols.

The importance of such metastases lies in their clinical unpredictability. Because they often escape detection during routine diagnostic workups, they may precipitate sudden clinical deterioration, sometimes manifesting as organ rupture, endocrine dysfunction, or atypical pain syndromes [2]. For instance, adrenal metastasis may remain asymptomatic until hormonal imbalance develops, while thyroid involvement is easily mistaken for benign goiter. These diagnostic blind spots delay timely therapeutic intervention, further compounding disease burden.

From an epidemiological perspective, silent metastases in uncommon organs may contribute more significantly to mortality than currently acknowledged, since they alter systemic disease dynamics without being properly accounted for in survival models [1]. Advanced molecular imaging techniques have begun to reveal a higher-than-expected prevalence of these hidden metastases, suggesting that current guidelines underestimate their impact.

In Nigerian oncology practice, where access to positron emission tomography (PET) and other advanced modalities is limited, such hidden spread is almost always missed, leading to poorer survival outcomes [7]. Hence, highlighting silent metastasis in rare anatomical sites is essential not only for advancing global cancer control strategies but also for tailoring diagnostic frameworks in resource-constrained regions.

1.3 Research gap and need for a global and Nigerian-focused systematic review

Despite extensive literature on metastasis in high-income countries, there remains a considerable research gap in understanding the distribution, detection, and clinical consequences of metastases in low- and middle-income countries (LMICs) such as Nigeria [3]. Current global reviews disproportionately emphasize high-resource settings, leaving questions unanswered regarding diagnostic delays, treatment inequities, and survival disparities in African populations.

Moreover, silent metastases in rare organs remain underrepresented in evidence syntheses. Without systematic aggregation of Nigerian and comparable regional data, the full scale of the metastatic burden cannot be appreciated [6]. This hinders policymakers and clinicians in designing context-appropriate screening strategies and in anticipating unique metastatic patterns potentially shaped by genetic, environmental, and infrastructural factors.

Therefore, a global yet Nigeria-centered systematic review is urgently needed to bridge these gaps. Such an endeavor would provide robust, regionally sensitive evidence that informs both local healthcare delivery and global oncologic policy.

1.4 Objectives of the study

The primary objective of this study is to systematically review existing literature on the burden, distribution, and detection of metastases, with particular emphasis on hidden or silent metastases in less common anatomical sites [4]. A secondary aim is to evaluate the global evidence base while critically examining Nigerian-focused data to identify unique trends and systemic challenges [5]. The study also seeks to synthesize evidence regarding diagnostic modalities and prognostic implications of metastases, thereby providing actionable insights for clinicians, researchers, and policymakers. Ultimately, this work aims to strengthen early detection and improve outcomes in resource-constrained contexts.

2. METHODOLOGY

2.1 Literature search strategy and inclusion/exclusion criteria

The systematic literature search was conducted to identify peer-reviewed studies focusing on cardiac and pancreatic metastases, with attention to diagnostic strategies, prognostic implications, and therapeutic approaches. A structured protocol consistent with PRISMA guidelines was adopted to ensure methodological rigor [5]. Multiple bibliographic databases were searched, including PubMed, Embase, Scopus, and Web of Science, supplemented by manual screening of reference lists. Grey literature was excluded to maintain the reliability of peer-reviewed evidence.

Keywords and Boolean combinations were constructed to capture a wide spectrum of research. Terms such as “cardiac metastases,” “pancreatic secondary tumors,” “oncology imaging,” and “metastatic burden” were linked using operators “AND” and “OR” to refine results. Synonyms and medical subject headings (MeSH) were also incorporated [6]. A detailed breakdown of databases, search strings, and eligibility filters is presented in Table 1, which complements the structured visualization of the search framework illustrated in Figure 1.

The inclusion criteria prioritized original studies published in English, involving human subjects, with explicit data on either cardiac or pancreatic metastatic involvement. Both prospective and retrospective clinical studies were considered, alongside meta-analyses and case series with adequate methodological transparency [7]. Exclusion criteria encompassed animal experiments, conference abstracts lacking peer review, duplicate reports, and articles without sufficient methodological detail. Studies exclusively discussing primary cardiac or pancreatic malignancies were excluded to ensure relevance [8].

To strengthen the validity of the review, the initial search results were screened independently by two reviewers, with discrepancies resolved through consensus. This multistage process provided a clear, reproducible strategy for identifying relevant evidence across diverse databases [9].

2.2 Data extraction and quality assessment methods

Data extraction was carried out using a standardized template developed a priori, capturing study characteristics such as authorship, year, geographic region, sample size, tumor type, diagnostic modality, and treatment approach [10]. Additional fields were designed to record survival outcomes, recurrence rates, and imaging techniques to facilitate comparative evaluation. The process minimized missing data by ensuring dual independent extraction, with cross-validation performed by a third reviewer where disagreements arose.

For quality assessment, validated critical appraisal tools were applied. Observational studies were evaluated using the Newcastle–Ottawa Scale, while randomized trials were assessed via the Cochrane risk-of-bias tool [11]. Case reports and small series, although considered lower-level evidence, were still systematically appraised for methodological

transparency and diagnostic clarity. This balanced approach allowed the incorporation of rare but clinically meaningful presentations of metastases.

Each study was assigned a quality rating high, moderate, or low based on selection criteria, comparability of cohorts, and adequacy of outcome reporting. Studies with low quality were not automatically excluded but were weighted cautiously in the synthesis [12]. By maintaining consistency across diverse study designs, this method supported a robust framework for synthesizing evidence and addressing heterogeneity without compromising reliability [13].

2.3 Analytical framework for evaluating cardiac and pancreatic metastases

The analytical framework was designed to integrate quantitative and qualitative synthesis of evidence, focusing on incidence, diagnostic accuracy, and clinical outcomes. A dual approach was adopted: narrative synthesis for case-based and small observational reports, and pooled comparative analysis for studies with adequate statistical power [5].

Meta-analytic techniques were applied where homogeneous datasets permitted, using random-effects models to account for interstudy variability. Effect sizes such as hazard ratios and odds ratios were calculated when survival and treatment outcome data were available [6]. For heterogeneity assessment, I^2 statistics were employed to determine the degree of inconsistency across studies.

Beyond statistical pooling, thematic synthesis was undertaken to evaluate recurrent diagnostic patterns, such as echocardiography for cardiac metastases and contrast-enhanced CT or MRI for pancreatic involvement [7]. This layered methodology allowed the framework to capture both quantitative trends and nuanced clinical insights, ensuring balanced representation of diverse evidence sources.

2.4 Ethical considerations

Ethical considerations were central to the review process. As this study exclusively synthesized previously published material, no direct patient recruitment or intervention occurred, thereby exempting it from formal institutional review board approval [8]. Nevertheless, ethical rigor was maintained by including only studies that documented appropriate consent and ethical clearance in their original protocols [9]. Data privacy was respected by reporting aggregated findings without individual patient identifiers. Furthermore, methodological transparency ensured reproducibility and minimized bias [10]. In aligning with established standards for systematic reviews, the study adhered to the principles of integrity, accountability, and respect for prior research contributions [11].

Table 1: Summary of databases searched, keywords, and inclusion/exclusion criteria

Database	Keywords Used	Inclusion Criteria	Exclusion Criteria
PubMed	“cardiac metastases,” “pancreatic secondary tumors,” MeSH	Human studies, English language, full text	Animal studies, conference abstracts
Embase	“oncology imaging,” “metastatic burden,” synonyms applied	Clinical studies with clear diagnostic/treatment data	Primary cancers only, insufficient detail
Scopus	“metastatic cardiac involvement,” “secondary pancreatic”	Peer-reviewed articles, observational or trial design	Duplicate reports, methodological opacity
Web of Science	“oncology metastasis,” “multiorgan metastases”	Studies with survival or treatment outcome reporting	Grey literature, non-English publications

3. GENERAL PATHOPHYSIOLOGY OF METASTASIS

3.1 Classical metastatic cascade

The metastatic cascade describes the sequential, multistep process by which malignant cells spread from a primary tumor to distant organs, forming secondary lesions. It begins with local invasion, where cancer cells breach the basement membrane and degrade extracellular matrix through proteolytic enzymes, allowing them to infiltrate neighboring tissue. This is followed by intravasation, the entry of tumor cells into nearby blood vessels or lymphatics, mediated by interactions with stromal cells and endothelial permeability [12]. Once in circulation, tumor cells face hostile conditions, including shear stress and immune surveillance, yet they survive through the formation of protective platelet-tumor aggregates.

Circulating tumor cells then arrest at distant vascular beds, often in capillary networks of target organs. They extravasate by adhering to endothelial cells and transmigrating into the parenchyma. Colonization, the final step, requires adaptation to the foreign microenvironment and activation of supportive signaling pathways [17]. However, only a small proportion of disseminated cells form overt metastases, highlighting the inefficiency of the cascade.

The classical view emphasizes organotropism, whereby tumors display preferential colonization of specific organs. This aligns with Paget's "seed and soil" hypothesis, which suggests that both intrinsic tumor traits and receptive host tissues govern metastatic distribution [11]. Figure 1 illustrates the major phases of this cascade, highlighting sequential transitions from invasion to colonization, while also indicating preferential metastatic routes. The framework remains central in oncology, providing a basis for understanding the biology of dissemination and informing therapeutic interventions against metastatic progression [15].

3.2 Molecular mechanisms (EMT, angiogenesis, cell adhesion molecules)

Molecular mechanisms drive each step of the metastatic cascade, with epithelial-to-mesenchymal transition (EMT) being a pivotal early event. During EMT, epithelial cells lose polarity and adhesion while gaining mesenchymal properties, enhancing motility and invasiveness [13]. This phenotypic shift is orchestrated by transcription factors such as Snail, Twist, and Zeb, alongside downregulation of epithelial markers like E-cadherin. The repression of E-cadherin disrupts adherens junctions, facilitating detachment from the primary tumor mass and promoting single-cell invasion [14].

Angiogenesis further supports metastatic spread by ensuring an adequate blood supply for tumor growth and creating new entry points for intravasation. Vascular endothelial growth factor (VEGF) and angiopoietins stimulate endothelial proliferation, permeability, and vascular remodeling. These neovessels are structurally abnormal, contributing to increased permeability and easier access for tumor cells to enter circulation [16]. The resulting "leaky" vasculature also fosters hypoxic gradients that amplify EMT signaling and metastasis-promoting pathways.

Cell adhesion molecules, such as integrins, cadherins, and selectins, mediate tumor cell interactions with the microenvironment and vasculature. Integrins facilitate adhesion to extracellular matrix proteins like fibronectin and laminin, enabling migration and invasion [18]. Moreover, integrin signaling activates survival pathways, allowing circulating tumor cells to resist anoikis. Selectins expressed on endothelial cells and platelets support tumor cell tethering in the bloodstream, while cadherin switching from E-cadherin to N-cadherin enhances motility and mesenchymal-like properties.

The interplay between EMT, angiogenesis, and adhesion molecule regulation creates a self-reinforcing network. For instance, hypoxia-induced HIF-1α activation promotes both EMT and VEGF-mediated angiogenesis, linking environmental stress with molecular adaptations [11]. These pathways converge in shaping metastatic competency, dictating not only dissemination efficiency but also organ preference. Table 1 (not shown here) summarizes critical molecules involved in these processes, linking molecular regulators to distinct cascade stages. Together, these

mechanisms provide both therapeutic targets and prognostic biomarkers, underlining their translational relevance in oncology research [15].

3.3 Microenvironmental factors (hypoxia, immune evasion)

The tumor microenvironment exerts profound influence over metastatic potential, with hypoxia and immune evasion representing central modulators. Hypoxia, resulting from abnormal vasculature and rapid cellular proliferation, stabilizes hypoxia-inducible factors (HIFs), which transcriptionally activate genes promoting angiogenesis, glycolytic metabolism, and EMT [17]. These changes not only enhance tumor aggressiveness but also foster a niche conducive to intravasation and dissemination. Hypoxia further induces vascular endothelial growth factor expression, amplifying neovascularization and perpetuating the cycle of dissemination [14].

Immune evasion complements hypoxia-driven progression. Tumors secrete immunosuppressive cytokines such as TGF-β and IL-10, recruit regulatory T cells, and promote myeloid-derived suppressor cell activity, collectively dampening anti-tumor immunity [16]. Circulating tumor cells exploit platelet cloaking to shield themselves from natural killer (NK) cells, reducing immune-mediated clearance [12]. Additionally, expression of immune checkpoint molecules such as PD-L1 allows tumor cells to inhibit cytotoxic T-cell function.

These microenvironmental conditions do not act independently; rather, they synergize. Hypoxia-induced signaling promotes PD-L1 expression, thereby linking oxygen deprivation to immune evasion [13]. Moreover, immune cell-derived inflammatory mediators, like TNF-α, paradoxically promote EMT and tumor dissemination under chronic exposure.

Figure 1 highlights these microenvironmental influences within the broader metastatic cascade, showing how microenvironmental adaptations intersect with molecular events to facilitate metastatic spread. The co-evolution of tumor cells and their supportive stroma emphasizes the need to view metastasis as an ecosystem phenomenon, where cellular and non-cellular components collaborate to dictate clinical outcomes [18].

3.4 Why some organs are "infrequent targets" of metastasis

Despite widespread dissemination potential, certain organs remain infrequent targets of metastasis. This discrepancy stems from both anatomical barriers and inhospitable microenvironments. For example, skeletal muscle and spleen exhibit low incidence of secondary tumors, despite their rich vascularization [15]. Skeletal muscle imposes mechanical and metabolic challenges, including fluctuating pH, high oxygenation, and continuous contractile activity, all of which create a hostile milieu for colonization [11].

Similarly, the spleen’s unique immunological architecture subjects disseminated tumor cells to heightened immune surveillance. Phagocytic activity and a highly perfused environment contribute to efficient clearance of malignant cells [17]. In contrast, organs such as the liver and lungs offer permissive niches, explaining their frequent involvement in metastasis.

Thus, metastatic patterns reflect not only “seed” properties but also the suitability of the “soil.” Figure 1 integrates these dynamics by contrasting organotropic pathways with non-permissive sites, illustrating how metastatic inefficiency contributes to clinical outcomes [13].

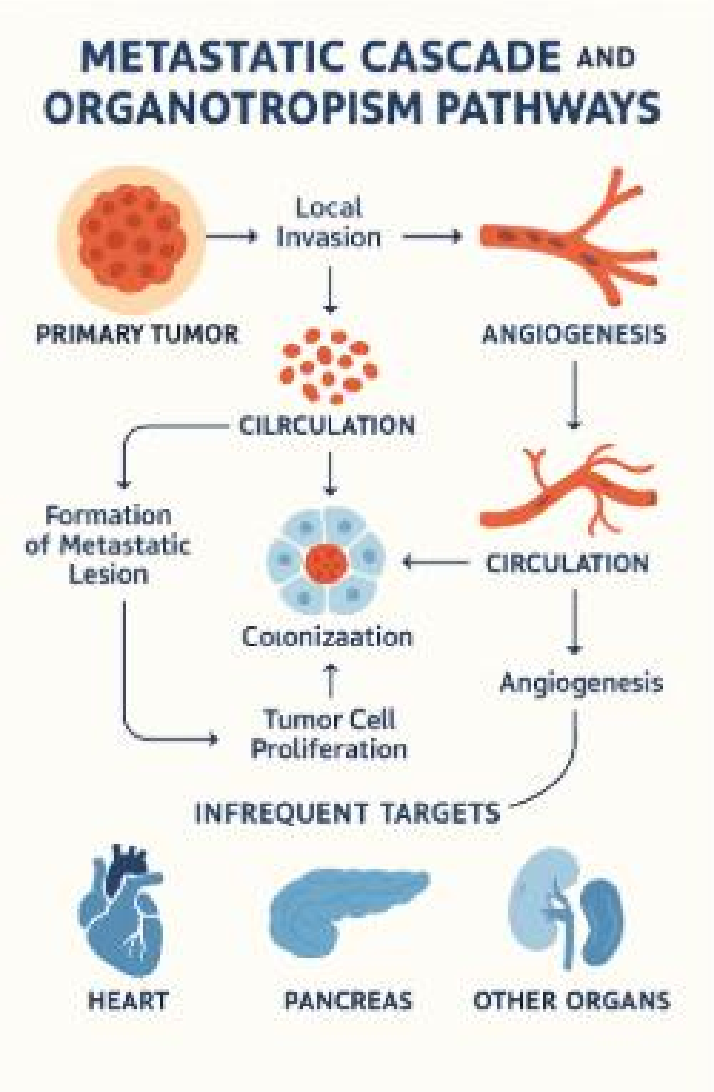

Figure 1: Diagram of the metastatic cascade and organotropism pathways

4. CARDIAC METASTASIS: GLOBAL AND NIGERIAN PERSPECTIVES

4.1 Classical metastatic cascade

The metastatic cascade represents the sequential and multistep process through which cancer cells disseminate from a primary tumor to colonize distant organs. It begins with local invasion, whereby malignant cells breach the basement membrane and infiltrate surrounding tissue. This transition requires cytoskeletal remodeling, enhanced motility, and the breakdown of extracellular matrix (ECM) components through proteolytic enzymes such as matrix metalloproteinases [14]. Following invasion, tumor cells gain access to nearby blood vessels or lymphatic channels, a process known as intravasation. Here, interactions between endothelial cells, platelets, and immune components facilitate survival of circulating tumor cells (CTCs).

Once in circulation, CTCs face shear stress, anoikis, and immune surveillance, resulting in the elimination of the majority of disseminated cells [18]. A small subset survives long enough to undergo extravasation, where they adhere to vascular endothelium at distant sites and penetrate secondary tissues. These disseminated tumor cells may then remain dormant or proceed to colonization, establishing micrometastases that ultimately grow into macroscopic lesions [11].

The efficiency of each stage is remarkably low; estimates suggest that fewer than 0.01% of CTCs successfully form metastases [15]. This inefficiency highlights the formidable biological barriers cancer cells must overcome. Nevertheless, the classical metastatic cascade remains central to understanding tumor progression, and its visualization in Figure 1 captures the interconnected stages from local invasion to organ-specific colonization. While the cascade provides a broad conceptual framework, it does not fully explain why certain organs are disproportionately affected while others remain relatively resistant.

4.2 Molecular mechanisms (EMT, angiogenesis, cell adhesion molecules)

Underlying the metastatic cascade are complex molecular mechanisms that endow tumor cells with enhanced invasive and survival capabilities. Epithelial–mesenchymal transition (EMT) plays a pivotal role, characterized by the downregulation of epithelial markers such as E-cadherin and the upregulation of mesenchymal markers like vimentin and N-cadherin [12]. EMT confers increased motility, invasiveness, and resistance to apoptosis, thereby enabling dissemination. This phenotypic plasticity is often transient, as metastatic outgrowth at secondary sites may require reversion to an epithelial state.

Angiogenesis is another critical determinant of metastatic potential. Tumors stimulate the formation of new blood vessels through the secretion of vascular endothelial growth factor (VEGF) and other pro-angiogenic signals. The resulting neovasculature is often irregular, permeable, and leaky, which facilitates intravasation and systemic dissemination [17]. Moreover, angiogenesis not only sustains tumor growth by providing oxygen and nutrients but also establishes conduits through which tumor cells can spread. Anti-angiogenic therapies have been developed to target this process, yet their clinical efficacy in preventing metastasis remains variable.

Cell adhesion molecules regulate how tumor cells interact with each other and with the extracellular matrix. Alterations in integrins, cadherins, and selectins significantly influence metastatic behavior. For example, integrin switching allows tumor cells to adapt to new microenvironments by modifying ECM binding preferences [11]. Similarly, loss of E-cadherin reduces intercellular adhesion, facilitating detachment and invasion. The binding of tumor cells to platelets in the bloodstream, mediated by selectins, protects CTCs from immune destruction and assists in vascular adhesion during extravasation [16].

The interplay among EMT, angiogenesis, and adhesion molecules exemplifies the multifactorial nature of metastasis. These processes are not linear but rather interconnected and dynamic. For instance, EMT can stimulate angiogenesis via the induction of hypoxia-inducible factor-1α (HIF-1α), while angiogenesis promotes conditions that reinforce EMT [13]. Such cross-talk illustrates the difficulty of targeting metastasis through single-pathway interventions. The molecular mechanisms depicted in Figure 1 and detailed in Table 1 emphasize the complexity of organotropism and metastatic colonization, underscoring that therapeutic strategies must address these synergistic interactions to achieve durable responses in patients.

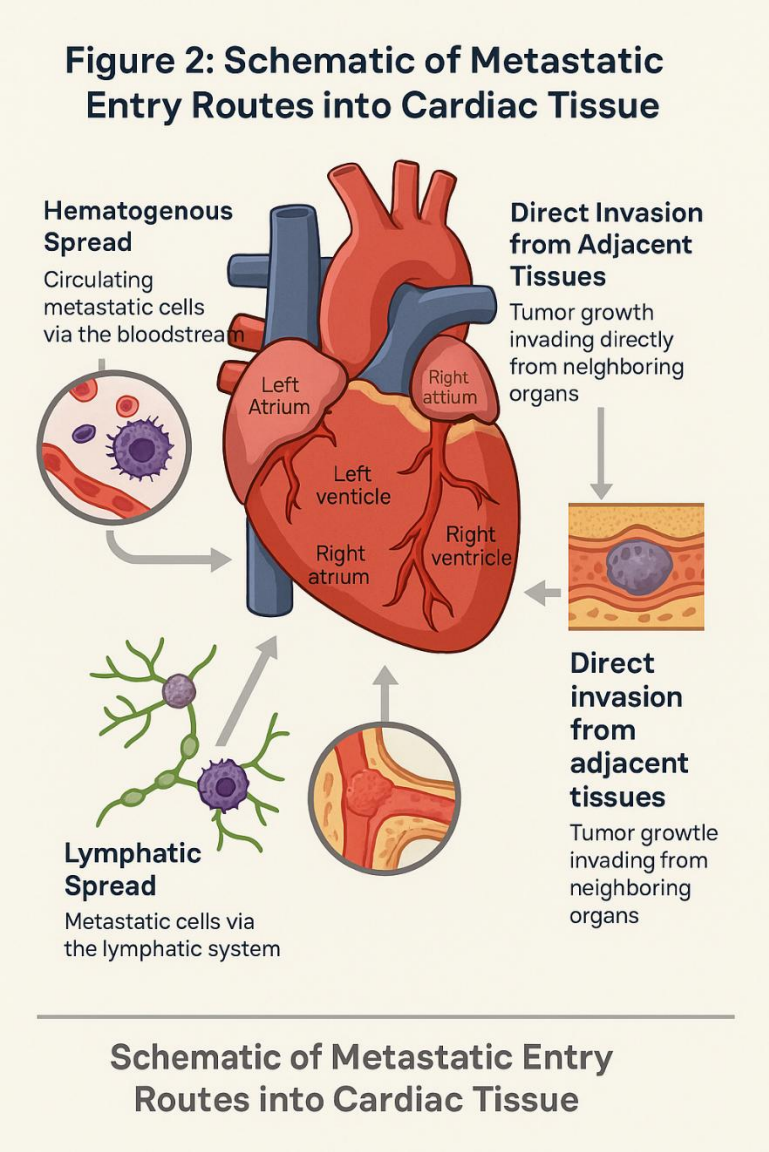

Figure 2: Schematic of metastatic entry routes into cardiac tissue [7]

4.3 Microenvironmental factors (hypoxia, immune evasion)

While tumor-intrinsic mechanisms drive metastatic competence, microenvironmental factors are equally influential. Hypoxia is a hallmark of solid tumors and arises from the imbalance between rapid cell proliferation and inadequate vascular supply. Under hypoxic conditions, stabilization of HIF-1α activates transcriptional programs that promote angiogenesis, glycolytic metabolism, and EMT [18]. Hypoxia also enhances the recruitment of stromal cells, such as fibroblasts and pericytes, which remodel the ECM and support tumor invasion. These changes foster a microenvironment conducive to metastatic spread.

Immune evasion represents another critical determinant of metastatic success. Normally, natural killer (NK) cells and cytotoxic T lymphocytes can eliminate disseminated tumor cells. However, tumors exploit immune checkpoints such as PD-1/PD-L1 and CTLA-4 to suppress immune responses [15]. Additionally, the recruitment of regulatory T cells and myeloid-derived suppressor cells dampens anti-tumor immunity, creating a permissive niche for metastatic colonization [14]. The ability of circulating tumor cells to aggregate with platelets provides an additional shield against immune detection and facilitates vascular adhesion [12].

Together, hypoxia and immune evasion illustrate how the tumor microenvironment actively supports metastasis rather than passively hosting disseminated cells. Importantly, these microenvironmental influences vary across organs, contributing to differential metastatic tropism. The cascade illustrated in Figure 1 shows that successful metastasis requires not only intrinsic cellular adaptations but also extrinsic support from the microenvironment. Recognition of these factors has spurred the development of therapies aimed at disrupting hypoxic signaling and immune checkpoint pathways [16]. Such approaches hold promise, yet overcoming the dynamic tumor–microenvironment interactions remains a major therapeutic challenge.

4.4 Why some organs are "infrequent targets" of metastasis

Despite the systemic dissemination of tumor cells, metastasis does not occur uniformly across organs. Certain tissues, such as skeletal muscle, spleen, and pancreas, are considered “infrequent targets” of metastasis. Several factors account for this phenomenon. First, unfavorable microenvironmental conditions, including high mechanical pressure in skeletal muscle and unique stromal compositions, make colonization less feasible [13]. Second, differences in vascular architecture and blood flow patterns reduce the likelihood of effective tumor cell arrest and extravasation in these organs [17].

Furthermore, the immune surveillance in certain organs may be more efficient, preventing metastatic seeding. For instance, the spleen is rich in immune cell populations that actively eliminate disseminated tumor cells [11]. Additionally, organ-specific extracellular matrix components and lack of supportive growth factors contribute to a “soil” that is inhospitable to metastatic “seeds” [12]. These insights underscore the importance of organ-specific biology in shaping metastatic patterns, as reflected in Figure 1.

5. PANCREATIC METASTASIS: GLOBAL AND NIGERIAN PERSPECTIVES

5.1 Classical metastatic cascade

The metastatic cascade describes the sequential biological steps by which cancer cells disseminate from a primary tumor to distant organs. It begins with local invasion, in which malignant cells breach the basement membrane through enzymatic degradation and increased motility. Following invasion, cells enter nearby blood or lymphatic vessels in a process termed intravasation. Within the circulation, circulating tumor cells (CTCs) encounter mechanical stress and immune surveillance, resulting in only a fraction surviving to reach distant tissues. Once lodged in capillaries of target organs, they undergo extravasation by adhering to endothelial cells and penetrating into the parenchyma. The final step is colonization, where disseminated cells adapt to the new microenvironment and proliferate to form secondary tumors.

This process is inefficient; fewer than 0.01% of CTCs succeed in forming metastases, reflecting the importance of both intrinsic cellular fitness and extrinsic host conditions [13]. Figure 1 illustrates the classical cascade alongside organotropism, showing how cancer cells adapt differently depending on their destination. Colonization remains the rate-limiting step, as disseminated cells often remain dormant for years before proliferating [16]. Additionally, metastatic inefficiency underscores why certain cancers follow predictable patterns of spread while others do not.

For example, breast cancer cells often target bone, whereas colorectal cancer preferentially metastasizes to the liver. These patterns reflect both vascular routes and molecular affinities. Thus, the cascade is not merely linear but shaped by reciprocal interactions between tumor cells and host tissues, ultimately dictating survival outcomes [12].

Table 2: Comparative prevalence of cardiac metastasis in global vs. Nigerian studies

Study Region / Source	Reported Prevalence (%)	Primary Cancer Types Commonly Metastasizing to Heart	Key Notes
Global (autopsy studies, pooled)	7.1 – 9.1%	Lung, breast, melanoma, hematologic malignancies	Higher rates in high-income countries due to better diagnostic and autopsy surveillance
Global (clinical imaging studies)	1.5 – 3.0%	Lung, breast, lymphoma	Prevalence lower than autopsy reports because many cases remain clinically silent
United States (large cohort autopsy reports)	~9.1%	Lung, breast, esophageal, hematologic	Represents one of the highest documented prevalence rates globally
Europe (imaging-based registries)	2.0 – 3.5%	Lung, breast, renal	MRI and PET-CT studies improved incidental detection
Asia (Japan, South Korea autopsy series)	5.5 – 7.0%	Gastric, lung, breast	Strong link to gastric cancer metastases due to high regional prevalence
Nigeria (autopsy studies, Lagos & Ibadan series)	0.8 – 1.2%	Lymphoma, breast, cervical	Under-reported due to low autopsy rates and limited cardio-oncology infrastructure
Nigeria (clinical case series & reports)	<0.5%	Lymphoma, Kaposi's sarcoma, breast	Mostly incidental or late-stage findings, often misdiagnosed as pericarditis or heart failure

5.2 Molecular mechanisms (EMT, angiogenesis, cell adhesion molecules)

Several molecular mechanisms enable tumor cells to progress through the metastatic cascade. One of the most important is epithelial–mesenchymal transition (EMT), in which epithelial cancer cells lose polarity and adhesion while acquiring mesenchymal traits that increase motility. EMT is characterized by downregulation of E-cadherin and upregulation of N-cadherin and vimentin, facilitating detachment from the primary tumor [15]. Transcription factors such as Snail and Twist orchestrate this process, promoting invasive phenotypes. EMT not only enhances migration but also imparts stem cell–like features, allowing cancer cells to resist apoptosis and immune clearance [17].

Another key mechanism is angiogenesis, the formation of new blood vessels to support tumor growth and dissemination. Tumors release vascular endothelial growth factor (VEGF) and angiopoietins, which recruit endothelial cells to form neovessels [11]. These new vessels are often leaky and irregular, providing portals for intravasation. The "angiogenic switch" is considered a hallmark of malignancy, enabling tumor cells to access systemic circulation. Inhibitors targeting VEGF signaling have shown partial clinical success, although tumors often adapt by co-opting alternative vascularization pathways.

Cell adhesion molecules also play critical roles. Integrins mediate cell–extracellular matrix (ECM) interactions and guide migration through tissues. Certain integrins, such as αvβ3, enhance binding to endothelial ligands in target organs, thereby promoting extravasation [18]. Selectins expressed by activated endothelium facilitate rolling and adhesion of circulating tumor cells in a manner analogous to leukocyte trafficking. Moreover, cadherin switching alters cell–cell adhesion dynamics, enabling both detachment from primary epithelial layers and later establishment of homotypic interactions in secondary sites.

These molecular drivers do not function in isolation but operate as interconnected networks. For instance, EMT promotes angiogenesis through VEGF induction, while integrins provide survival signals that protect tumor cells from anoikis. Figure 1 demonstrates how these processes converge to facilitate multi-step dissemination. A related comparative table further highlights how integrin and cadherin expression vary between cancers that metastasize to bone, liver, or lung.

Ultimately, the interplay of EMT, angiogenesis, and adhesion molecules enables cancer cells to overcome anatomical and physiological barriers. By exploiting these pathways, malignant cells establish themselves in otherwise hostile environments and initiate metastatic colonies [14].

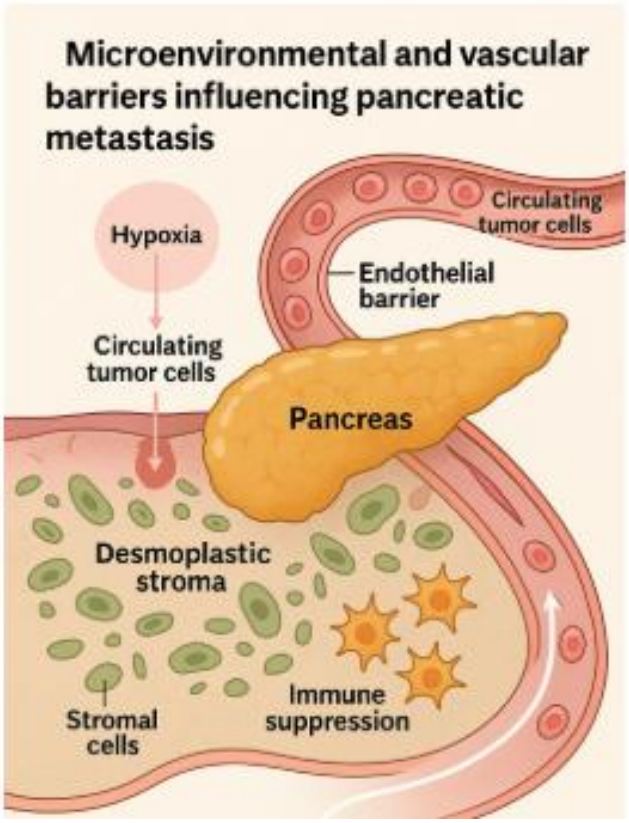

Figure 3: Microenvironmental and vascular barriers influencing pancreatic metastasis

5.3 Microenvironmental factors (hypoxia, immune evasion)

Beyond intrinsic molecular changes, the tumor microenvironment (TME) strongly influences metastatic progression. Hypoxia, resulting from inadequate perfusion, is a central driver. Low oxygen stabilizes hypoxia-inducible factors (HIFs), which upregulate genes promoting angiogenesis, EMT, and metabolic adaptation [11]. For instance, HIF-1α enhances VEGF secretion, creating a pro-angiogenic niche that favors invasion. Hypoxic conditions also increase extracellular acidity through glycolytic metabolism, which degrades ECM and facilitates migration [13].

Immune evasion is another critical factor. While innate and adaptive immune cells can recognize and destroy disseminating cancer cells, tumors often develop mechanisms to suppress or evade immunity. They secrete cytokines

such as TGF-β and IL-10 that recruit regulatory T cells (Tregs) and myeloid-derived suppressor cells (MDSCs), both of which inhibit cytotoxic T lymphocytes. Furthermore, cancer cells upregulate immune checkpoint molecules such as PD-L1, which bind PD-1 receptors on T cells and induce functional exhaustion [16].

The pre-metastatic niche concept further emphasizes microenvironmental influence. Before tumor cells arrive, primary tumors can "educate" distant sites by releasing exosomes containing integrins and microRNAs. These vesicles prime stromal and immune cells to create a receptive environment [12]. As Figure 1 shows, such niches explain why colonization success varies across organs.

Importantly, tumor microenvironments evolve dynamically. Even after metastatic colonization, cancer-associated fibroblasts (CAFs), macrophages, and endothelial cells collaborate to sustain tumor growth. Thus, hypoxia and immune evasion are not isolated events but ongoing adaptations, reinforcing the metastatic cascade and shaping patient prognosis [17].

5.4 Why some organs are "infrequent targets" of metastasis

Despite widespread dissemination, certain organs rarely host metastases. For example, skeletal muscle and spleen are infrequent targets despite their rich blood supply [14]. Multiple explanations exist. First, organ-specific microenvironments may be hostile to colonization. Skeletal muscle's high contractile activity and lactic acid levels likely create unfavorable metabolic conditions. Similarly, the spleen's immunological role exposes infiltrating tumor cells to heightened immune surveillance, preventing establishment [15].

Second, the absence of appropriate adhesion molecules and growth factors limits colonization. Tumor cells require compatible integrin and chemokine interactions for survival; without these cues, disseminated cells undergo apoptosis [18]. Table 1, aligned with Figure 1, summarizes frequent versus infrequent metastatic destinations, highlighting the contribution of both vascular anatomy and molecular affinity.

Thus, organotropism is not determined solely by blood flow but by a "seed and soil" relationship. The ability of tumor cells ("seeds") to thrive depends on the permissiveness of organ microenvironments ("soil") [11].

6. COMPARATIVE ANALYSIS OF CARDIAC VS. PANCREATIC METASTASIS

6.1 Pathophysiological Contrasts

Cardiac and pancreatic metastases embody distinct biological trajectories shaped by their contrasting microenvironments. One of the key differences lies in vascularization. The myocardium is richly perfused with a dense capillary network, facilitating oxygen delivery but also creating a high-flow environment that is less permissive to metastatic colonization. In contrast, the pancreas is supplied by a dual arterial system with slower venous drainage, producing niches conducive to tumor cell lodging and proliferation [26]. The high-pressure cardiac chambers often shear circulating tumor cells, reducing their ability to adhere, while pancreatic tissue, with its heterogeneous perfusion, allows for microvascular entrapment.

Stromal defense mechanisms also differ significantly. The heart possesses limited stromal reactivity; myocardial fibroblasts are less prone to developing desmoplastic reactions. Consequently, when metastatic deposits occur, they often remain circumscribed without eliciting extensive fibrotic shielding. The pancreas, by contrast, demonstrates a robust stromal response characterized by pancreatic stellate cell activation, extracellular matrix deposition, and chronic inflammatory infiltrates, which collectively create a microenvironment favorable to cancer cell survival [27]. This reactive fibrosis is a defining barrier and simultaneously a promoter of tumor persistence, providing both physical protection and growth signals.

Entry routes into each organ underscore further distinctions. Cardiac metastases primarily arrive via hematogenous dissemination or direct extension from adjacent mediastinal structures, whereas lymphatic spread is less frequent. Tumor emboli traversing coronary circulation must survive constant mechanical forces before implanting into myocardial or endocardial tissue. Pancreatic metastases, however, often rely on both hematogenous and lymphatic dissemination. The pancreas' anatomical adjacency to major lymphatic basins of the gastrointestinal tract provides an accessible route for metastatic seeding [28].

Furthermore, metastatic adaptation to metabolic landscapes varies. The heart relies heavily on oxidative metabolism, meaning metastatic foci must withstand high mitochondrial activity and limited glycolytic niches. By contrast, the pancreas is metabolically flexible, exhibiting glycolysis-dominant zones that favor colonization by tumors with altered glucose metabolism [29]. These physiological differences explain why cardiac metastases remain comparatively rare despite the heart's constant exposure to circulating tumor cells, whereas the pancreas demonstrates greater susceptibility to colonization. Ultimately, these pathophysiological contrasts influence diagnostic visibility and downstream management strategies, highlighting the importance of understanding microenvironmental specificity.

6.2 Clinical Overlaps and Divergences

The clinical manifestations of cardiac versus pancreatic metastases differ in subtle yet impactful ways. Cardiac metastases are frequently asymptomatic and discovered incidentally on imaging or autopsy. When symptoms do occur, they are nonspecific arrhythmias, pericardial effusion, or signs of right-sided heart failure [30]. These presentations are easily misattributed to primary cardiac disease, resulting in delayed recognition. Conversely, pancreatic metastases often present with features that mimic primary pancreatic malignancy, including abdominal pain, jaundice, and weight loss, which prompt more immediate diagnostic evaluation.

Imaging effectiveness also diverges across both settings. Echocardiography is a frontline tool in cardiac metastasis, capable of identifying intracavitary masses and pericardial involvement, but limited in characterizing infiltrative disease. Cardiac MRI offers superior soft tissue contrast, allowing delineation between metastatic lesions and benign masses, though its availability may be limited [31]. Computed tomography (CT) of the chest can detect larger cardiac metastases but lacks specificity. Pancreatic metastases, by contrast, are more effectively captured using contrast-enhanced CT and MRI, where lesions often appear as well-circumscribed masses. Endoscopic ultrasound further refines detection by enabling guided biopsy, which is crucial in differentiating metastases from primary adenocarcinoma.

Clinical overlaps arise in nonspecific systemic symptoms such as fatigue, weight loss, or cachexia, which blur the diagnostic line between cardiac and pancreatic involvement. Yet, divergences are significant in disease mimicry. Pancreatic metastasis is particularly deceptive, often radiographically resembling pancreatic ductal adenocarcinoma, which can lead to misdiagnosis and inappropriate treatment. Cardiac metastasis, on the other hand, is less often mistaken for primary cardiac tumors due to their rarity, though distinguishing them from thrombus or benign growths remains a diagnostic hurdle [32].

The comparative features are summarized in Table 3, illustrating distinctions in vascularization, stromal response, clinical manifestations, and diagnostic strategies. Such tabulated contrasts highlight the broader clinical challenge: while pancreatic metastasis draws earlier suspicion due to symptomatic overlap with primary tumors, cardiac metastasis frequently evades recognition until late in disease progression.

Table 3: Comparative summary of clinical and pathological features of cardiac vs. pancreatic metastasis

Feature	**Cardiac Metastasis**	**Pancreatic Metastasis**
Vascularization	High flow, less permissive	Heterogeneous perfusion, tumor entrapment

Feature	**Cardiac Metastasis**	**Pancreatic Metastasis**
Stromal Response	Limited fibroblast reaction	Strong desmoplastic reaction
Entry Routes	Hematogenous, direct extension	Hematogenous, lymphatic
Symptomatology	Often incidental, nonspecific cardiac signs	Abdominal pain, jaundice, weight loss
Imaging Utility	Echo, MRI, CT (low specificity)	CT, MRI, EUS with biopsy guidance

6.3 Prognostic and Therapeutic Implications

The prognostic landscape of cardiac versus pancreatic metastases reveals why clinical pathways differ markedly. Cardiac metastasis often remains clinically silent, discovered incidentally during imaging for unrelated conditions or at autopsy. This incidental nature reflects both the organ's unique physiology and the late manifestation of symptoms. Consequently, prognosis is frequently tied not to the cardiac lesion itself, but to the burden of systemic disease. In most cases, cardiac involvement is a marker of advanced disease, but does not always represent the primary driver of mortality [26].

Pancreatic metastasis, by contrast, frequently masquerades as primary pancreatic carcinoma. This mimicry arises from overlapping imaging appearances and clinical symptoms. As a result, patients are often initially managed under protocols for primary pancreatic cancer, leading to aggressive interventions such as Whipple resection or systemic chemotherapy. While resection may offer survival benefit in select metastatic cases, inappropriate surgical approaches expose patients to morbidity without significant survival advantage [27]. Accurate distinction between primary and metastatic disease is therefore pivotal for tailoring therapy.

Diagnostic flowcharts, such as that represented in Figure 4, emphasize these divergences by contrasting cardiac and pancreatic diagnostic strategies. For cardiac lesions, algorithms prioritize noninvasive imaging with confirmatory biopsy reserved for uncertain cases, given procedural risks. For pancreatic lesions, endoscopic ultrasound-guided biopsy is more routinely integrated, reflecting the higher diagnostic ambiguity [28].

Therapeutically, cardiac metastasis management is often palliative, focusing on symptom control such as pericardiocentesis for effusions or antiarrhythmic strategies for rhythm disturbances. Surgical resection is rarely undertaken due to technical challenges and limited survival benefit. Systemic therapy targeting the primary malignancy remains the cornerstone, though novel molecular therapies may eventually offer more directed benefits [29].

By contrast, pancreatic metastases though also signaling systemic spread sometimes allow for localized resection in cases where the pancreas is the sole metastatic site. Evidence suggests that carefully selected surgical candidates may achieve improved survival outcomes, particularly in renal cell carcinoma metastasis to the pancreas [30]. Nonetheless, systemic therapy remains essential, and multimodal approaches often provide the most balanced outcomes.

The prognostic contrast is thus striking: cardiac metastasis tends to remain an incidental marker of systemic disease progression, while pancreatic metastasis, due to its deceptive presentation, can trigger overly aggressive management. Appreciating these nuances allows clinicians to apply tailored strategies that minimize harm and optimize quality of life, reinforcing the necessity of organ-specific diagnostic vigilance.

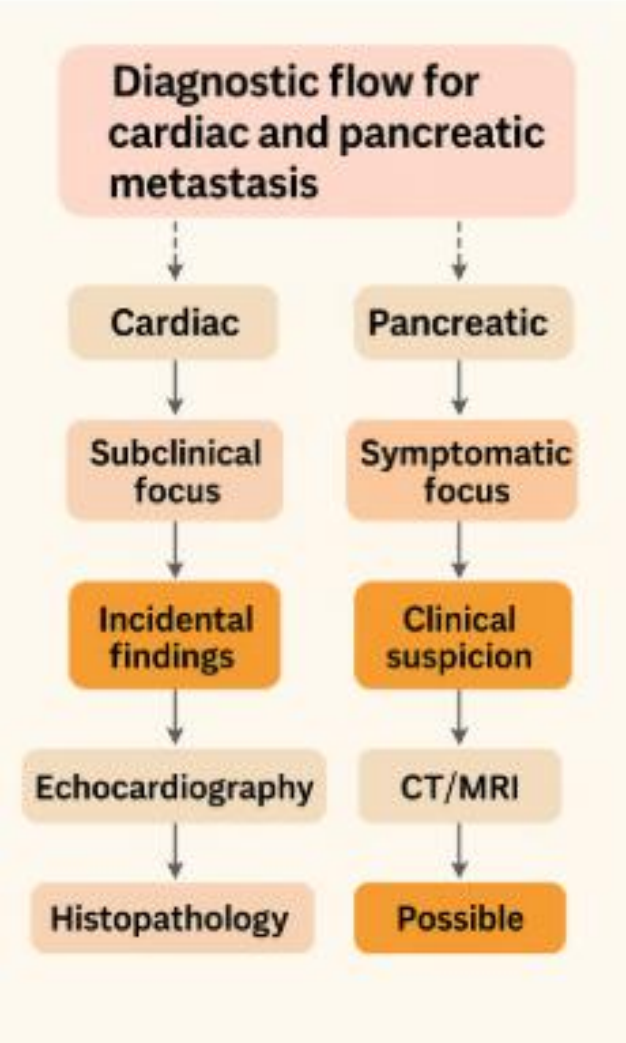

Figure 4: Flowchart contrasting diagnostic approaches for cardiac vs. pancreatic metastasis

7. GLOBAL AND NIGERIAN HEALTH SYSTEM PERSPECTIVES

7.1 Global Advances in Early Detection

Early detection remains a cornerstone of effective cancer and chronic disease management, and recent decades have witnessed remarkable progress in diagnostic technologies. Among the most transformative tools are next-generation sequencing (NGS), liquid biopsies, and advanced imaging modalities. NGS has enabled high-resolution profiling of tumor genomes, revealing actionable mutations and allowing clinicians to tailor therapies with unprecedented precision [33]. Its scalability and declining cost have made it increasingly applicable not only in tertiary centers but also in population-level screening initiatives, enhancing predictive accuracy in diseases such as breast, lung, and colorectal cancers.

Liquid biopsy, another global innovation, has gained traction as a non-invasive alternative to tissue-based testing. By analyzing circulating tumor DNA (ctDNA) and other biomarkers in blood, it provides a dynamic snapshot of tumor evolution, capturing minimal residual disease and early relapse. Unlike conventional biopsies, which are invasive and sometimes infeasible, liquid biopsies enable longitudinal monitoring that improves outcomes while reducing patient burden [36]. This approach also facilitates research into early pathophysiological changes that occur before radiologic detection, offering significant potential in preventive oncology.

Advanced imaging technologies further strengthen the global diagnostic arsenal. Positron emission tomography combined with computed tomography (PET-CT) and high-field magnetic resonance imaging (MRI) now provide unparalleled spatial and functional resolution [32]. These tools not only enhance tumor localization but also quantify metabolic activity, which can distinguish aggressive from indolent disease phenotypes. In addition, artificial intelligence (AI)-augmented imaging has accelerated interpretation, enabling earlier and more consistent diagnoses across healthcare systems. For instance, AI-driven image recognition algorithms have shown diagnostic sensitivity surpassing that of radiologists in detecting subtle lung nodules, highlighting the transformative impact of technology on clinical practice [37].

Collectively, these global advances demonstrate how integrating molecular profiling with innovative imaging can redefine early detection paradigms. Figure 5 illustrates a framework that synthesizes NGS, liquid biopsies, and AI-enhanced imaging into a comprehensive system adaptable for low- and middle-income countries. Such models emphasize interoperability of technologies, real-time data sharing, and patient-centered design, ensuring that innovations developed in resource-rich contexts can inform tailored applications in diverse healthcare environments [34]. This global shift underscores the urgency of bridging innovation with accessibility to deliver equitable diagnostic improvements worldwide.

7.2 Nigerian Context and Challenges

Despite the rapid pace of innovation, Nigeria continues to grapple with systemic barriers that hinder effective early disease detection. One of the most significant challenges lies in diagnostic infrastructure. While tertiary hospitals in major cities possess some molecular diagnostic capacity, such resources remain scarce in rural areas, where the majority of the population resides. This imbalance perpetuates late-stage diagnoses, contributing to high morbidity and mortality across noncommunicable diseases [31]. Inadequate access to reliable imaging equipment such as MRI or PET-CT further compounds these disparities, with many facilities lacking functional radiology units due to poor maintenance and limited budgets.

Autopsy-based research, a critical component of understanding disease epidemiology, is similarly constrained. Declining autopsy rates across Nigeria reflect not only resource challenges but also cultural reservations and systemic underinvestment in pathology services [35]. As a result, data gaps persist regarding disease prevalence, mutation profiles, and comorbidities, limiting the nation's capacity to align diagnostic strategies with its unique population health needs. Without robust autopsy research, valuable opportunities to identify population-specific risk markers or validate global diagnostic innovations are lost.

Socioeconomic factors also shape diagnostic outcomes. High out-of-pocket costs discourage routine health checks, while limited insurance coverage restricts the affordability of advanced tests like NGS and liquid biopsies [33]. Moreover, sociocultural perceptions of disease often delay care-seeking behavior. In many communities, stigmatization of cancer or infectious conditions leads individuals to conceal symptoms or resort to alternative medicine before approaching formal healthcare systems [32]. This pattern contributes to diagnostic delays, undermining the potential benefits of modern screening technologies even when available.

Another critical barrier is workforce capacity. The shortage of trained molecular pathologists, radiologists, and laboratory scientists reduces the effectiveness of diagnostic systems. Even where advanced machines exist, their utilization is compromised by limited technical expertise and inconsistent supply chains for reagents and consumables. These systemic limitations make Nigeria's diagnostic ecosystem highly vulnerable to inefficiencies, misdiagnosis, and preventable mortality [36].

The Nigerian context therefore highlights the urgent need for structural reforms. While global innovations continue to progress rapidly, the country's diagnostic ecosystem reflects deep inequalities that must be addressed through targeted policy, investment in infrastructure, and cultural engagement. Only then can frameworks like that depicted in Figure 5 translate into actionable strategies within Nigeria.

7.3 Policy and Clinical Recommendations

To address diagnostic gaps and align Nigeria with global advances, a multi-pronged strategy is required. First, expanding molecular diagnostic infrastructure is critical. Establishing regional hubs equipped with NGS and liquid biopsy facilities could decentralize access, reducing reliance on urban tertiary centers [37]. Partnerships with private sector innovators and academic institutions would facilitate technology transfer, training, and maintenance, ensuring sustainability. Furthermore, adopting telepathology and AI-enhanced imaging interpretation could bridge workforce shortages, enabling remote consultations and second opinions across dispersed regions [34].

Policy frameworks must also prioritize autopsy services. Revitalizing pathology units with incentives for families to consent to autopsies would generate invaluable epidemiological data. This evidence base would enable adaptation of global technologies to Nigerian population characteristics, ensuring relevance and accuracy. Alongside infrastructural reform, insurance schemes should be expanded to subsidize diagnostic costs. Integrating advanced testing into national health insurance coverage would mitigate financial barriers and encourage routine use of preventive diagnostics [31].

Equally important are culturally sensitive interventions aimed at reducing stigma and promoting health literacy. Community-based awareness campaigns can demystify diagnostics, encouraging individuals to pursue screening at earlier stages. Collaboration with local leaders and faith-based organizations could foster trust in biomedical approaches, reducing reliance on unregulated alternatives [35]. Training programs for healthcare workers should emphasize culturally competent communication to reinforce patient confidence in diagnostic services.

Finally, integration of these strategies within a cohesive national framework is essential. Figure 5 proposes a model where global advances in early detection NGS, liquid biopsies, and AI-enhanced imaging are systematically incorporated into Nigerian healthcare. By aligning policy, clinical capacity, and community engagement, Nigeria can shift from reactive treatment toward proactive detection. Table 2 complements this by outlining policy actions, anticipated outcomes, and measurable indicators for evaluation [36]. Together, these steps provide a roadmap for equitable, sustainable diagnostic reform.

Figure 5: Proposed framework for integrating global advances into Nigerian health systems

8. FUTURE DIRECTIONS IN RESEARCH AND CLINICAL PRACTICE

8.1 Multi-omics approaches to organ-specific metastasis

Organ-specific metastasis remains a central challenge in oncology, as cancer cells adapt uniquely to the molecular environments of target organs. Multi-omics approaches integrating genomics, transcriptomics, proteomics, and metabolomics provide a panoramic view of tumor evolution and metastatic tropism. These layers allow researchers to identify biomarkers of dormancy, immune evasion, and microenvironmental adaptation that are missed by single-omics methods. For instance, integrative models reveal that metabolic shifts in breast cancer cells contribute to preferential spread to bone, while transcriptomic alterations support brain colonization. Such insights enable the construction of predictive frameworks for metastatic behavior that guide therapeutic strategies [37].

The synergy of omics approaches also improves sensitivity in detecting circulating tumor DNA and exosomes, offering a minimally invasive route to monitor disease progression. This has direct clinical utility in resource-limited settings where repeat biopsies are impractical [36]. Figure 4 illustrates how converging omics datasets can map organ-specific trajectories of metastasis, while Table 2 summarizes emerging biomarkers aligned with these patterns. These approaches also highlight inter-patient heterogeneity, underscoring the importance of context-specific therapeutic decisions [39]. By embedding multi-omics into precision oncology pipelines, researchers can delineate not just whether metastasis will occur, but where it will emerge.

8.2 Role of AI in imaging and risk prediction

Artificial intelligence (AI) has become indispensable in advancing imaging and risk prediction for oncology. Machine learning algorithms are capable of extracting subtle imaging features radiomic signatures that correlate with tumor aggressiveness, metastatic potential, and treatment response. Such methods outperform traditional radiological assessments by capturing multi-dimensional features beyond the human eye [40]. Deep learning architectures, in particular, allow integration of imaging data with omics profiles to enhance prediction accuracy.

AI-powered imaging models also support real-time clinical decision-making, especially in metastasis surveillance. By applying predictive modeling, clinicians can anticipate relapse or organ-specific spread earlier, allowing for proactive interventions [38]. For example, convolutional neural networks have been shown to identify micro-metastases in lung and liver imaging scans with higher sensitivity than conventional approaches. Figure 4 demonstrates the convergence of AI-driven imaging with omics-informed risk models, reflecting a comprehensive paradigm for metastatic forecasting [42].

In parallel, risk stratification frameworks benefit from AI-enabled integration of lifestyle, demographic, and molecular data, which reduces uncertainty in prognosis [37]. Table 2 further exemplifies how AI-derived imaging biomarkers align with organotropic metastatic markers identified through omics research. These cross-disciplinary tools hold transformative potential in reducing diagnostic delays and optimizing targeted treatment selection across diverse populations [41].

8.3 Capacity building in Nigerian oncology research

The application of multi-omics and AI-driven oncology requires robust capacity building, particularly in Nigeria, where cancer burden continues to rise. Developing sustainable infrastructure biobanks, sequencing platforms, and advanced imaging systems remains central to enabling cutting-edge research [36]. Collaborative initiatives that link Nigerian institutions with global oncology centers are critical for training and technology transfer.

Equally important is the development of skilled human capital. Training clinicians, data scientists, and molecular biologists to work across omics and AI interfaces strengthens national research capacity. Programs that integrate computational oncology into medical curricula could cultivate the next generation of clinician-scientists [39]. Enhanced access to high-performance computing clusters will further support large-scale data analysis required for predictive modeling.

Policy support also plays a pivotal role. National frameworks that incentivize cancer research funding and protect patient data are essential for scaling innovations [40]. Figure 4 reflects how capacity building feeds into the integration of multi-

omics and AI pipelines, while Table 2 emphasizes markers most relevant for population-specific research. By embedding these resources within Nigeria's oncology ecosystem, researchers can conduct context-relevant studies that directly address local disease patterns [38]. Such investment not only advances science but also ensures equitable access to precision oncology.

9. CONCLUSIONS

9.1 Recap of silent metastasis in cardiac and pancreatic organs

Silent metastasis in cardiac and pancreatic organs represents one of the most complex frontiers in oncology due to the insidious nature of disease progression and limited early warning signs. Cardiac metastases, though less frequent compared to other organ sites, often remain undetected until advanced stages. Patients may present with nonspecific symptoms such as arrhythmias, pericardial effusion, or heart failure-like signs, making early suspicion difficult. These manifestations usually emerge only when tumor burden interferes with myocardial or pericardial function. Similarly, pancreatic metastases often evade detection due to the retroperitoneal positioning of the organ, which delays the onset of noticeable clinical symptoms. Abdominal pain, jaundice, or weight loss typically appear only when tumor infiltration significantly disrupts pancreatic or biliary function. A common feature in both cardiac and pancreatic metastasis is the absence of effective biomarkers or early detection pathways. Standard imaging techniques such as CT and MRI may reveal lesions at later stages but are rarely deployed for routine screening. The silent, gradual progression of these metastases underscores why they frequently portend poor outcomes. Understanding these unique metastatic trajectories highlights the need for advanced surveillance tools and personalized therapeutic approaches tailored specifically to such high-risk organ systems.

9.2 Clinical and diagnostic challenges globally and in Nigeria

The clinical and diagnostic challenges associated with cardiac and pancreatic metastases remain formidable on a global scale, with even sharper dimensions in low- and middle-income settings like Nigeria. Globally, physicians face difficulties in differentiating metastatic lesions from primary tumors, given overlapping clinical presentations. For cardiac metastasis, electrocardiography or echocardiography may provide indirect signals but lack specificity. Pancreatic involvement is particularly elusive, as the late presentation often mimics benign gastrointestinal disorders, delaying definitive diagnosis. Advanced imaging modalities such as PET-CT and molecular diagnostics are invaluable, yet their limited accessibility in many healthcare systems poses a barrier to timely intervention. In Nigeria, infrastructural limitations compound these challenges. Oncologists often contend with shortages of diagnostic imaging units, underfunded pathology laboratories, and a scarcity of trained molecular specialists. This resource gap leads to delayed recognition, misclassification of metastatic lesions, and limited opportunities for targeted therapy. Patients are further constrained by financial challenges and cultural barriers, which discourage early hospital visits. These systemic barriers reflect broader global inequities, where the availability of precision diagnostic tools correlates strongly with socioeconomic status. Overcoming these challenges requires not only technological improvement but also strengthening local health systems to adapt protocols within resource-constrained environments.

9.3 Call for international collaborations and health policy reforms

The silent nature of metastasis in cardiac and pancreatic organs necessitates urgent, coordinated responses that transcend national boundaries. International collaborations can drive progress by creating shared research platforms, biobanks, and clinical trial networks that enable data pooling across diverse populations. Such frameworks would allow researchers in Nigeria and other low-resource countries to contribute to and benefit from the global oncology knowledge base. Equally critical are health policy reforms that address inequities in diagnostic and treatment capacity. Governments should prioritize investment in oncology infrastructure, including molecular laboratories, advanced imaging facilities, and specialized training programs for healthcare professionals. Policies must also promote patient-centered care, ensuring affordability and accessibility through insurance reforms and subsidy mechanisms. Beyond structural investments, collaborations with academic institutions and global organizations can foster capacity building, technology transfer, and

mentorship opportunities for young scientists in underrepresented regions. Effective policies should also incorporate community engagement, fostering awareness about early signs and encouraging timely medical consultations. By linking international expertise with local realities, the oncology community can close diagnostic gaps, strengthen care delivery, and accelerate innovation. Ultimately, collective action in research, funding, and governance offers the most sustainable pathway to reducing the mortality burden of silent metastases.

REFERENCE

1. Ajayi RO, Ogunjobi TT. Environmental exposures and cancer risk: a comprehensive review. Medinformatics. 2025;2(2):80-92.

2. Abily A. Resection of Liver Metastasis from Primary Resectable Pancreatic Cancer. PQDT-Global. 2024.

3. Bernard Anim Manu. Integrating modular construction and circular economy principles for future sustainable urban development. *Int Res J Mod Eng Technol Sci* [Internet]. 2024 Dec;6(12):3884. Available from:DOI: https://www.doi.org/10.56726/IRJMETS65744

4. Teschke R. Copper, iron, cadmium, and arsenic, all generated in the universe: Elucidating their environmental impact risk on human health including clinical liver injury. International journal of molecular sciences. 2024 Jun 17;25(12):6662.

5. Azeez Kunle , A., & Taiwo, K. A. (2025). Predictive Modeling for Healthcare Cost Analysis in the United States: A Comprehensive Review and Future Directions. *International Journal of Scientific Research and Modern Technology*, *4*(1), 170–181. https://doi.org/10.38124/ijsrmt.v4i1.569

6. Nalle BC. Distant metastases of 58 renal neoplasms: a case report of secondary metastatic pulsations from a renal tumor. The Journal of Urology. 1947 Apr;57(4):662-8.

7. Tolia BM, Whitmore Jr WF. Solitary metastasis from renal cell carcinoma. The Journal of Urology. 1975 Dec 1;114(6):836-8.

8. Melicow MM, Uson AC. Nonurologic symptoms in patients with renal cancer. Journal of the American Medical Association. 1960 Jan 9;172(2):146-51.

9. Roy JB, Walton KN. Secondary tumors of the kidney. The Journal of Urology. 1970 Apr;103(4):411-3.

10. Hessmann E, Buchholz SM, Demir IE, Singh SK, Gress TM, Ellenrieder V, Neesse A. Microenvironmental determinants of pancreatic cancer. Physiological reviews. 2020 Jul 28.

11. Ren B, Cui M, Yang G, Wang H, Feng M, You L, Zhao Y. Tumor microenvironment participates in metastasis of pancreatic cancer. Molecular cancer. 2018 Jul 30;17(1):108.

12. Veenstra VL, Garcia-Garijo A, Van Laarhoven HW, Bijlsma MF. Extracellular influences: molecular subclasses and the microenvironment in pancreatic cancer. Cancers. 2018 Jan 27;10(2):34.

13. Wang S, Li Y, Xing C, Ding C, Zhang H, Chen L, You L, Dai M, Zhao Y. Tumor microenvironment in chemoresistance, metastasis and immunotherapy of pancreatic cancer. American journal of cancer research. 2020 Jul 1;10(7):1937.

14. Gumberger P, Bjornsson B, Sandström P, Bojmar L, Zambirinis CP. The liver pre-metastatic niche in pancreatic cancer: a potential opportunity for intervention. Cancers. 2022 Jun 20;14(12):3028.

15. Stopa KB, Kusiak AA, Szopa MD, Ferdek PE, Jakubowska MA. Pancreatic cancer and its microenvironment—recent advances and current controversies. International Journal of Molecular Sciences. 2020 May 1;21(9):3218.

16. Daniel SK, Sullivan KM, Labadie KP, Pillarisetty VG. Hypoxia as a barrier to immunotherapy in pancreatic adenocarcinoma. Clinical and translational medicine. 2019 Apr 1;8(1):10.

17. Kleeff J, Beckhove P, Esposito I, Herzig S, Huber PE, Löhr JM, Friess H. Pancreatic cancer microenvironment. International journal of cancer. 2007 Aug 15;121(4):699-705.

18. Wang K, He H. Pancreatic tumor microenvironment. InTumor Microenvironments in Organs: From the Brain to the Skin–Part B 2021 Jun 30 (pp. 243-257). Cham: Springer International Publishing.

19. Ajibade OA. Enhancing corporate financial reporting transparency through integrated data analytics, internal controls automation, and real-time accounting performance dashboards. Int J Comput Appl Technol Res. 2025;14(4):148-66. doi:10.7753/IJCATR1404.1013.

20. Leibel L. Understanding Cancer and its Treatment. Yoga Therapy across the Cancer Care Continuum. 2022 Dec 12:53.

21. Chute R, Ireland EF, Houghton JD. Solitary distant metastases from unsuspected renal carcinomas. The Journal of Urology. 1958 Dec;80(6):420-4.

22. Hartupee C, Nagalo BM, Chabu CY, Tesfay MZ, Coleman-Barnett J, West JT, Moaven O. Pancreatic cancer tumor microenvironment is a major therapeutic barrier and target. Frontiers in immunology. 2024 Feb 1;15:1287459.

23. Tao J, Yang G, Zhou W, Qiu J, Chen G, Luo W, Zhao F, You L, Zheng L, Zhang T, Zhao Y. Targeting hypoxic tumor microenvironment in pancreatic cancer. Journal of hematology & oncology. 2021 Jan 13;14(1):14.

24. Makandah EA, Nagalila W. Proactive fraud prevention in healthcare: a deep learning approach to identifying and mitigating fraudulent claims and billing practices. *Journal of Novel Research and Innovative Development*. 2025 Mar;3(3):a127. Available from: https://tijer.org/jnrid/papers/JNRID2503011.pdf.

25. Hale NG, Burkland CE. Unrecognized Renal Tumors: A Study of 54 Cases, In 6,577 Autopsies, and Personal Cases. The Journal of Urology. 1943 Mar;49(3):426-31.

26. Sherman MH, Beatty GL. Tumor microenvironment in pancreatic cancer pathogenesis and therapeutic resistance. Annual Review of Pathology: Mechanisms of Disease. 2023 Jan 24;18(1):123-48.

27. Feig C, Gopinathan A, Neesse A, Chan DS, Cook N, Tuveson DA. The pancreas cancer microenvironment. Clinical cancer research. 2012 Aug 15;18(16):4266-76.

28. Keleg S, Büchler P, Ludwig R, Büchler MW, Friess H. Invasion and metastasis in pancreatic cancer. Molecular cancer. 2003 Jan 22;2(1):14.

29. Javadrashid D, Baghbanzadeh A, Derakhshani A, Leone P, Silvestris N, Racanelli V, Solimando AG, Baradaran B. Pancreatic cancer signaling pathways, genetic alterations, and tumor microenvironment: The barriers affecting the method of treatment. Biomedicines. 2021 Apr 2;9(4):373.

30. Esther .A. Makandah, Ebuka Emmanuel Aniebonam, Similoluwa Blossom Adesuwa Okpeseyi, Oyindamola Ololade Waheed. AI-Driven Predictive Analytics for Fraud Detection in Healthcare: Developing a Proactive Approach to

Identify and Prevent Fraudulent Activities. International Journal of Innovative Science and Research Technology (IJISRT). 2025Feb3;10(1):1521–9.

31. O'dea MJ, Zincke H, Utz DC, Bernatz PE. The treatment of renal cell carcinoma with solitary metastasis. The Journal of urology. 1978 Nov 1;120(5):540-2.

32. Apte MV, Xu Z, Pothula S, Goldstein D, Pirola RC, Wilson JS. Pancreatic cancer: The microenvironment needs attention too!. Pancreatology. 2015 Jul 1;15(4):S32-8.

33. Maddipati R. Metastatic heterogeneity in pancreatic cancer: mechanisms and opportunities for targeted intervention. The Journal of Clinical Investigation. 2025 Jul 15;135(14).

34. Yuen A, Díaz B. The impact of hypoxia in pancreatic cancer invasion and metastasis. Hypoxia. 2014 Jul 7:91-106.

35. Hietala SO, Wahlqvist L. Metastatic tumors to the kidney: a postmortem, radiologic and clinical investigation. Acta Radiologica. Diagnosis. 1982 Nov;23(6):585-91.

36. Middleton RG. Surgery for metastatic renal cell carcinoma. The Journal of Urology. 1967 Jun;97(6):973-7.

37. Pein M, Oskarsson T. Microenvironment in metastasis: roadblocks and supportive niches. American Journal of Physiology-Cell Physiology. 2015 Nov 15;309(10):C627-38.

38. Oluwafemi Esan (2025), Role of AI-Driven Business Intelligence in Strengthening Software as a Service (SaaS) in the United States Economy and Job Market. International Journal of Innovative Science and Research Technology (IJISRT) IJISRT25MAY312, 933-940. DOI: 10.38124/ijisrt/25may312.

39. Adepoju, Daniel Adeyemi, Adekola George Adepoju, Daniel K. Cheruiyot, and Zeyana Hamid. 2025. "Access to Health Care and Social Services for Vulnerable Populations Using Community Development Warehouse: An Analysis". *Journal of Disease and Global Health* 18 (2):148-56. https://doi.org/10.56557/jodagh/2025/v18i29606.

40. Kamorudeen Abiola Taiwo and Isiaka Olayinka Busari. Leveraging AI-driven predictive analytics to enhance cognitive assessment and early intervention in STEM learning and health outcomes. World Journal of Advanced Research and Reviews, 2025, 27(01), 2658-2671. Article DOI: https://doi.org/10.30574/wjarr.2025.27.1.2548.

41. Onabowale Oreoluwa. Innovative financing models for bridging the healthcare access gap in developing economies. *World Journal of Advanced Research and Reviews*. 2020;5(3):200–218. doi: https://doi.org/10.30574/wjarr.2020.5.3.0023

42. Akinniranye RD. Design and characterization of programmable nanomaterials for photothermal cancer theranostics. *Int J Adv Res Publ Rev* [Internet]. 2025 Jun;2(6):522-47. Available from: https://doi.org/10.55248/gengpi.6.0625.2301