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Multimodal AI and Machine Learning for Predictive Risk Stratification, Early Detection, And Clinical Management of Pica: Integrating Etiological and Pathophysiological Biomarkers

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Abstract:

ABSTRACT

Pica is a clinically significant and often overlooked feeding and eating disorder in which individuals have a persistent urge to eat or chew non-nutritious or non-food items and is linked to nutritional, hematological, behavioral, and environmental issues. Human studies have regularly found links between pica and iron deficiency and anemia, as well as between changes in hematological parameters, decreased ferritin, and decreased zinc concentrations; toxic-element exposure may also be a part of certain behaviors (like geophagia). The review critically summarises the potential use of multimodal artificial intelligence (AI) and machine learning (ML) to support predictive risk stratification, early detection, and clinical management of pica, highlighting the importance of combining etiological and pathophysiological biomarkers, clinical, behavioural, toxicological and electronic health-record data. Biomarker evidence also indicates human exposure to multiple biomarkers together may be a more complete risk profile than single biomarkers, since there are human data from which to draw conclusions. AI and natural language processing could be used to identify undetected pica-related behaviors and track changes over time to clinical and laboratory data. However, there are still limitations in the development and validation of pica-specific AI models, and existing evidence from related conditions mainly methodologically supports the use of AI. Further studies are needed on large, prospective, diverse human cohorts, standardized pica phenotyping, longitudinal assessment of biomarkers, explainable AI, external validation, and prospective clinical assessment. Finally, multimodal AI should be used as a clinically interpretable decision support system, not as an independent diagnostic system.

Keywords: Pica; Multimodal Artificial Intelligence; Machine Learning; Biomarkers; Risk Stratification; Early Detection.

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1. INTRODUCTION

Pica is a clinically significant feeding and eating disorder where there is a persistent intake of non-nutritive, non-food items like ice, soil, clay, chalk, starch, paper, hair, soap, ash, and other substances[1]. Pica can be seen in all age groups and clinical populations, but is often underdiagnosed and may not be reported voluntarily by the individual ingesting the substance, and can have a variety of clinical presentations depending on the ingested substance, age, pregnancy, nutritional status, developmental characteristics, psychiatric comorbidities, and the environment. Human studies have shown significant links between pica, exposure to potentially toxic elements, nutritional abnormalities, iron deficiency and alterations in hematological parameters, and specific patterns of pica, like geophagia, may be linked to other toxic elements. The results suggest that pica is not merely a behavioural phenomenon, but rather a multi-dimensional clinical phenotype related to nutritional, haematological, behavioural and environmental factors.

Figure 1: Pica[2]

The introduction of recent artificial intelligence (AI), machine learning (ML) and natural language processing (NLP) advances has opened new opportunities to combine different clinical information to assess individual risk. Demographic, behavioral, EHR, hematological, nutritional, toxicological, clinical, and longitudinal laboratory information can be potentially integrated in AI-driven approaches. This is especially significant with regard to pica as there is no single marker to diagnose the condition. Biomarkers of human exposure and/or studies have been associated with pica and include hemoglobin, ferritin, mean corpuscular volume (MCV), red-cell distribution width (RDW), blood lead, serum iron, transferrin-related indices, and zinc; the latter may be relevant for specific types of pica[3]. Meanwhile, human AI research has been conducted on three areas relevant to this project: the prediction of iron deficiency, anemia, and eating

disorders, and all these efforts illustrate the utility of ML and NLP to uncover clinically relevant patterns from laboratory and EHR data. But there are still not enough pica-specific multimodal AI models which are clinically validated. As such, there is a need to critically review human evidence to define the potential for multimodal AI to aid in the predictive risk stratification, early detection, etiological assessment, and clinical management of pica.

1.1 Background Information and Context

The traditional approach to pica diagnosis is based on the clinical history, direct questioning, behavior and the presence of associated nutritional and/or medical abnormalities. Patients may be unaware of the non-food ingestion, and clinical signs and symptoms are dependent on the substance ingested and underlying illness. There have been correlations reported between pica and iron deficiency, anemia, decreased ferritin, changes in MCV and RDW, decreased zinc, and increased blood lead levels (BLL) in geophagia[4]. The findings indicate a multifactorial etiology of pica, with nutrition, hematology, behavior and environment all playing a role. These heterogeneous data could be supplemented with clinical history and behavioral data, and combined with artificial intelligence (AI) and machine learning (ML) to uncover complex patterns and to estimate the risk of pica in individuals. Longitudinal ML analysis of biomarker changes over time, and the use of natural language processing (NLP) to detect pica-related behaviors from clinical notes, could further delineate these behaviors. While most previous human AI studies are focused on iron deficiency anemia and other eating disorders, they offer a framework for building and testing future AI models specific to pica.

1.2 Objectives of the Review

The key aims of this review are:

- To give a general background of pica as a multi-faceted clinical disorder with behavioural, nutritional, haematological, developmental, psychiatric and environmental factors.
- To synthesize human-based evidence on pica's association with etiological and pathophysiological biomarkers in human, especially Fe-deficiency, anemia, Zinc status and toxic elements exposure.
- To analyze the feasibility of using multimodal AI and ML to combine clinical, behavioural, laboratory, nutritional and toxicological data in the risk assessment of pica.
- To review human-based AI/ML research that is relevant to pica, such as those in the field of computational prediction of phenotypes associated with iron-deficiency, anemia.
- To verify whether NLP and EHR analysis could provide behavioral clues that might not be recorded in the traditional clinical assessment and help identify pica.

1.3 Importance of the Topic

The importance of pica is that eating non-food items over time can cause nutritional deficiencies, anemia, toxic-element exposure, gastrointestinal and other serious health consequences. Throughout human history, iron deficiency, and anemia, are the consistent biological factors

associated with pica, while in certain populations, abnormalities in zinc and exposure related biomarkers offer further clinical information[5]. Yet, pica is underdiagnosed, since there is no single laboratory marker to detect pica. The use of multimodal AI and machine learning holds promise by integrating clinical history, behavioral features, hematological and nutritional biomarkers, electronic health records, and exposure-related information to support the predictive risk stratification, early detection, and clinical management of the patient. Pica-specific AI research, however, is still in its infancy, and further large, human, prospective studies are needed, along with standardized phenotyping, explainable AI, and detailed clinical validation to create dependable decision-support AI systems.

2. HUMAN EVIDENCE ON PICA, BIOMARKERS, AND ARTIFICIAL INTELLIGENCE

Pica is a clinically diverse feeding and eating disorder that involves the persistent ingestion of non-nutritive, non-food substances. There are significant relationships between pica and iron deficiency, anemia, altered hematological parameters, and zinc deficiency, as well as exposure to potentially toxic elements, depending on the type of pica, that have been found in human studies[6]. With the recent developments of artificial intelligence (AI), machine learning (ML), and natural language processing (NLP), there are opportunities to incorporate these biological, behavioral, and clinical characteristics in predictive risk stratification and early detection. The potential value of AI in the field of pica, however, is limited and results from other fields, like the identification of iron deficiency or eating disorders should be seen as methodological evidence, not as evidence for pica. The section covers key advancements in human pica studies, relevant biomarkers, and the promise of AI/ML in predicting and managing pica in clinical settings.

2.1 Pica and Iron Deficiency

In human studies, one of the most consistent and potent biological relationships with pica is with iron deficiency. People with iron-deficiency can experience strange cravings, including the urge to eat ice (pagophagia). Pica has been shown to be common in humans with iron deficiency or iron depletion.

Figure 2: Pica and Iron Deficiency[7]

Barton et al. studied 262 non-pregnant adults who were either iron deficient or iron depleted, and found that about 45% of these had pica. The individuals with pica had lower hemoglobin and mean corpuscular volume (MCV) and higher red-cell distribution width (RDW) and platelet counts than did the individuals without pica, and had lower ferritin concentrations. The results indicate that this may be a more complex pattern including a range of haematological and iron markers, rather than just one individual abnormal marker.

There was also a strong correlation between pica and anemia in a human meta-analysis of over 16,000 people. Pica was related to higher incidence of anemia, lower levels of hemoglobin, hematocrit, and plasma zinc. The results indicate that iron related and hematological variables should be considered in the next models predicting pica risk[8].

Strengths

- Strong human evidence of the link between pica and iron deficiency and anemia
- Various haematological and biochemical parameters can be analysed.
- Iron related biomarkers are widely available in clinical practice.
- The use of longitudinal laboratory measurements may offer opportunities for early prediction.

Weaknesses

- Pica does not have a specific cause for iron deficiency.
- Anemia and lower ferritin stores may be due to many different conditions.
- Most studies have been observational
- However, the direction and cause of the relationship is not fully understood.
- There is variability in pica definitions and assessment techniques across studies.

Iron deficiency is thus a valuable risk-associated biomarker profile and not a diagnostic marker of pica per se. Further models for future use should integrate iron-related data with behavioral and clinical data[9].

2.2 Hematological and Nutritional Biomarkers

Routine hematological and nutritional measurements could be useful for risk assessment of pica as these would be obtained during the clinical evaluation. The hematological parameters that are important to be evaluated are hemoglobin, hematocrit, MCV, mean corpuscular hemoglobin, RDW, platelet count, and red blood cell indices. Ferritin, serum iron, transferrin saturation and total iron binding capacity are important iron related biomarkers.

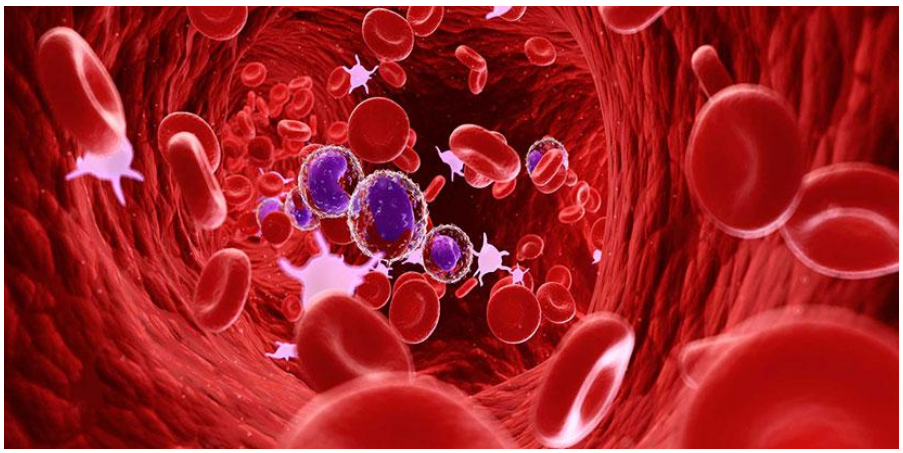

Figure 3: Hematological[10]

The combination of several biomarkers may provide greater predictive information than an individual measurement. For instance, if a patient presents with low haemoglobin, low MCV, elevated RDW, and low ferritin, then the low haemoglobin is suggestive of iron-deficiency pattern and a targeted assessment of pica might be indicated. Progressive changes may also be informative, as a progressive decline in ferritin or a change in red-cell indices may potentially indicate risk before severe anemia becomes apparent.

Another possible nutrient biomarker is zinc. Lower zinc levels have been reported in human research on those suffering from pica, and meta-analytic evidence confirms there is an association between pica and lower plasma zinc levels. But zinc status is influenced by various nutritional, physiological, and clinical factors, and is not sufficiently specific to be used as a stand-alone marker[11].

Strengths

- The majority of biomarkers can be measured in routine clinical investigations.
- Multiple parameters can be incorporated into predictive models.
- Longitudinal measurements can be used to show how things change over time.
- Hematological variables are easily obtained and relatively cheap.
- Some of the nutritional markers may offer data on possible underlying causes

Weaknesses

- Most of the biomarkers are not specific to pica.
- Several diseases and nutritional factors may impact nutritional status.
- The levels of the biomarkers can be affected by age, pregnancy, inflammation or other physiological factors
- Single measurements may not be suitable to represent chronic nutrition status.
- Further clinical evaluation is needed to confirm pica.

Thus, using a multiple marker approach, including haematological, iron-related and nutritional markers, might be more suitable than depending on a single laboratory marker[12].

2.3 Toxicological and Exposure-Related Biomarkers

The type of substance ingested and the medical risk of pica depends on what that person eats. This is especially significant in geophagia where people eat soil or clay that can contain potentially harmful elements. Among pregnant women, human study results have shown higher levels of blood lead among geophagia women than non-geophagia women. Human studies in children also have shown that children who suffer from pica have higher blood lead levels[13].

These results confirm that there are also toxicological implications to pica other than nutritional implications. This risk is likely to be different depending on the substance being used. For instance, the ingestion of ice can be linked mostly to nutritional or hematological deficiencies, while the ingestion of soil or clay can be linked to their toxicity due to the ingestion of toxic elements in the soil.

Based on suspected exposure and clinical context, potential exposure related biomarkers include blood lead, blood arsenic, blood mercury, and blood cadmium. Other clinically relevant parameters may include renal-function parameters, hepatic-function measurements, electrolyte abnormalities, and gastrointestinal findings.

Strengths

- Relevant exposure-associated abnormalities have been found in human studies, with clinical significance.
- Biomarkers may be objective indicators of toxic exposure.
- An individualized substance-specific assessment may help to refine the clinical risk characterization.
- Exposure biomarkers can be used to predict complications.

Weaknesses

- The toxicological risk depends greatly on the substance consumed.
- Not every patient with pica should be tested for toxins.
- The contamination of the environment is different in different regions.
- The exposure measurements may not always be available.
- The toxicity of the substance is not sufficient to prove the presence of pica.

Exposure variables should thus be included in future AI systems based on the particular pica phenotype and substance consumed, but not uniformly across all types of pica[14].

2.4 Human Artificial Intelligence and Machine-Learning Evidence Relevant to Pica

There is still limited research on the field of Pica using AI and ML. However, there is methodological value in human AI research in related clinical fields that will be helpful in the creation of future models of pica prediction.

Studies on humans have shown that machine-learning models can detect individuals at risk of iron-deficiency anemia without the presence of anaemia. Other studies that have analyzed laboratory data over time have demonstrated that deep-learning models can foretell iron-deficiency anemia months in advance of the standard diagnosis. The results suggest that clinical information can be gained from routinely collected laboratory trajectories, which could facilitate early clinical intervention[15].

Another potential use for NLP is that the clinical documentation of pica might not be in a structured diagnostic field. The use of NLP has been shown to be feasible in human studies to extract phenotypes related to eating disorders from EHRs. The same methods might be able to identify the descriptions of uncommon cravings or non-food items, like ice, soil, clay, starch, chalk or anything else.

Thus, a framework based on behavioral information, obtained using NLP, combined with laboratory biomarkers could serve as a basis for multimodal pica prediction.

Strengths

- Is able to combine several clinical and lab parameters
- Enables analysis of longitudinal electronic health records
- NLP can be used to obtain behavioral data from free-text medical records.
- May facilitate early identification of risk factors.
- May be able to create risk scores for each person.

Weaknesses

- There is few AI datasets dedicated to Pica.
- Existing models are mainly developed for related conditions
- Modelling may not be generalizable to the population
- Clinical documentation may be incomplete or inconsistent
- The black-box models could be hard to understand for clinicians.
- To make any prediction, prospective and external validation is necessary.

Current AI evidence should therefore be interpreted as supporting the feasibility of multimodal prediction rather than demonstrating that a validated AI system for pica already exists[16].

3. MULTIMODAL AI, RISK STRATIFICATION, AND CLINICAL APPLICATIONS

A novel approach to organising a range of human clinical information relating to pica is through the use of multimodal artificial intelligence (AI) and machine learning (ML). Multimodal AI can

integrate a variety of data, including demographic information, behavioral traits, hematological markers, nutritional biomarkers, toxicological data, electronic health records, and clinical-text data, which are analyzed separately in traditional methods[17]. The issues of multimodal data integration, population-specific risk stratification, predictive stratification, early detection, phenotype classification and longitudinal clinical monitoring are all major developments that are relevant to pica. While there are currently only limited AI models available for pica, recent developments in human-based AI research in iron deficiency and anemia, eating disorders and clinical NLP provide methodological frameworks for future pica-focused applications.

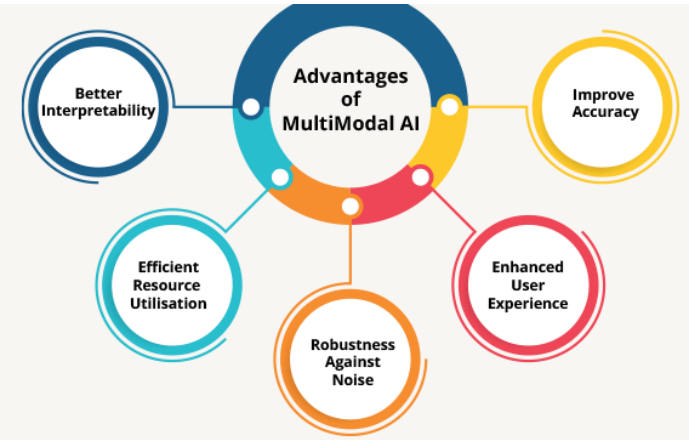

Figure 4: Multimodal artificial intelligence (AI)[18]

3.1 Multimodal Integration of Human Clinical and Biomarker Data

Pica is a heterogeneous condition and cannot be adequately characterized using a single clinical or biological variable. Human evidence suggests relationships with iron deficiency, anaemia, changes in haematological indices, zinc status and, depending on the substance ingested, exposure to a toxic element. Therefore, a future multimodal AI model may use a combination of demographic, clinical factors (age, sex, pregnancy status, developmental conditions, psychiatric history, medical diagnoses, medication exposure, and previous pica episodes) and behavioral factors (type of substance consumed, frequency, duration, quantity, craving intensity, and age at onset). Other biological variables, including hematological and nutritional parameters (hemoglobin, hematocrit, MCV, RDW, platelet count, ferritin, serum iron, transferrin saturation, total iron-binding capacity and zinc) may give further information.

Another crucial aspect of multimodal AI is clinical-text information. Structured electronic health records may not capture information regarding non-food ingestion in the physician's note, nursing documentation, dietary history, a psychiatric assessment, the emergency room or patient reported symptoms. Combining these various data sources may enable AI models to uncover intricate patterns that wouldn't be evident using traditional, single-variable screening. But even these would have to be standardized human data sets, correct handling of missing data, consistent measurements of biomarkers, and consideration of confounding factors[19].

3.2 Population-Specific and Phenotype-Based Risk Assessment

Pica may be seen in various age groups, clinical settings, and can be expressed in various ways as a function of pregnancy, developmental stages, nutritional status, psychiatric comorbidities, geographical environment, and cultural practices. Thus, AI models need to take into consideration the characteristics of populations, and not assume that a single risk profile is applicable to everyone. For instance, pica in a non-pregnant adult with iron deficiency can be different than pica in a child with developmental disorders, or in a pregnant woman.

Type of substance ingested also plays an important role in the risk assessment for phenotype. Ingestion of ice might be indicative of the association with iron deficiency only, and ingestion of soil or clay might be indicative of any additional toxicological risk. AI systems in the future could then be used to categorize patients based on the type of substance(s) ingested, nutritional status, toxicological exposure, and clinical complications associated with the substance(s) consumed[20]. Diverse human populations must be represented, as diet, environment, and access to health care as well as cultural practices and clinical documentation may differ significantly among populations. Models would be more generalizable if they were created from wider human datasets from other geographic and demographic populations.

3.3 Predictive Risk Stratification for Pica

One of the most promising areas of potential application of AI for pica research is predictive risk stratification. An AI system would not only forecast the likelihood of an individual needing targeted assessment for pica but would also intervene earlier than a formal diagnosis is made. Low-risk individuals may not show any significant abnormalities in behavior or in the biomarkers, while intermediate-risk individuals may show unexplained iron deficiency, low ferritin, low MCV or RDW, recurrent anemia, zinc deficiency, or history is suggestive. These could be targeted for clinical interrogation.

Persons with a high risk may have well-documented pica, severe nutritional abnormalities, well-documented significant anemia, and/or evidence of toxic-element exposure, gastrointestinal complications, or repeated health care visits due to pica[21]. This stratification may be useful to prioritize patients that need further evaluation and potentially reduce missed cases for clinicians. But, a risk classification should not be seen as a diagnosis as there are many other medical conditions that also show the same pica-associated markers.

3.4 Multimodal Biomarker-Based Early Detection

Specific attention should be given to early detection, as the non-food ingestion may not be spontaneously reported by patients. AI may offer a potential way of finding non-obvious biological or clinical indicators prior to the official diagnosis of pica. For instance, the combination of recurrent iron deficiency, decreasing ferritin level, low MCV, high RDW and a history of unusual cravings documented in the electronic health record could trigger a red flag alert. The composite pattern could lead to a suggestion of specific questioning on non-food intake.

The methodological support for this approach is given by human AI studies in related conditions. Machine learning models have shown to be good predictors of iron deficiency and iron deficiency anemia prior to the traditional diagnosis, based on clinical and longitudinal laboratory

data. However, the results are not directly used as evidence on the ability of AI to predict pica. Future models for pica need to establish if there is a possibility to differentiate between those who have pica and those who have similar laboratory abnormalities from other conditions.

3.5 Natural Language Processing and Behavioral Phenotype Detection

One potential element of multimodal AI is natural language processing (NLP), which is often included in the free text of clinical documentation instead of being documented in a structured diagnostic code and is a common way pica is described. This is because NLP may be able to describe the craving for ice, ingestion of soils or clay, ingestion of starch, ingestion of chalk or papers, recurrent craving for non-food items, unusual eating habits, and the symptoms associated with ingestion. These behavioral components could help better identify patients with pica that may otherwise not be documented.

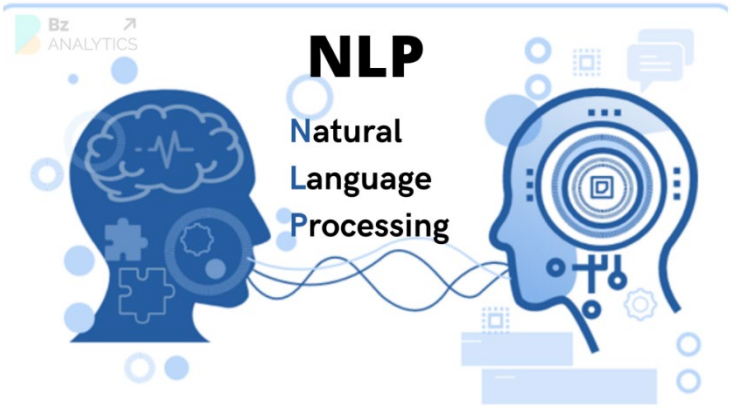

Figure 5: Natural Language Processing[22]

In fact, human research on eating disorders has shown that it is possible to retrieve clinically relevant behavioral data from eHR via NLP. This could be done with pica as well with behavioral data extracted and added to laboratory and clinical data. For instance, if clinical-text evidence of ice craving is present, along with low ferritin, low MCV, and high RDW, the possibility of an iron-deficiency associated pica phenotype must be considered. But NLP models need careful validation as clinical notes may contain incomplete, ambiguous information or information relevant to only a particular context.

3.6 AI-Based Clinical Management and Longitudinal Monitoring

AI can be used not just for early detection and risk prediction, but also for clinical management and long-term monitoring. After the diagnosis of pica, AI might be useful to describe the most probable underlying clinical profile and guide clinicians in the choice of investigations. For instance, pica with low ferritin, low MCV and high RDW may suggest an iron-deficiency associated phenotype, while geophagia with anemia and elevated blood lead may suggest toxicological risk associated with possible exposure[23].

Longitudinal AI might also track the changes in biomarkers and clinical symptoms after the intervention. Pica has been reported to resolve or improve after correction of iron deficiency in

human studies for a variety of clinical situations. So future models may be able to analyze baseline and follow-up ferritin, hemoglobin, MCV, RDW, nutrition markers, and behavioral symptoms to determine if the risk of pica is reducing. When laboratory parameters return to normal, but the pica continues, a need for further behavioral, psychiatric, developmental, or multidisciplinary assessment might be identified[24].

3.7 Explainable and Clinically Interpretable AI

For clinical use of AI in pica, explainability is a must. Clinicians should be aware of the reasons for the classification of increased pica risk. A probability score alone with no explanation might not be very clinically useful and may predispose to over-reliance on an automated system. Explainable AI can determine the relative importance of individual predictors, such as ferritin, hemoglobin, MCV, RDW, zinc, clinical-text indicators or exposure history[25].

For instance, an interpretable model may suggest that low levels of ferritin and abnormal red-cell indices were key factors underlying the predicted risk, and clinical data on non-food-cravings backed this up. This type of explanation would make it possible for clinicians to decide whether the prediction is clinically plausible or not and whether they need to conduct further assessment. Ex explainable AI can thus enhance transparency, clinician trust, patient-informed decision making and mitigate black-box prediction risks.

4. INTEGRATED MULTIMODAL AI FRAMEWORK FOR ETIOLOGICAL AND PATHOPHYSIOLOGICAL RISK STRATIFICATION OF PICA

An integrated multimodal AI framework could provide a comprehensive approach for identifying individuals at increased risk of pica by combining diverse human-derived clinical, behavioral, laboratory, nutritional, and toxicological information[26]. Pica is unlikely to be attributed to any single biomarker as its expression can include nutritional deficiencies, hematological abnormalities, developmental and/or psychiatric factors, pregnancy, environmental exposures, and substance-specific risks. Hence, the possibility of creating a multimodal model by combining demographic and clinical data with information related to pica-related behaviors, such as type of non-food substance, frequency, duration, quantity, intensity of craving, and previous episodes. Such integration could enable identification of complex patterns that may not be apparent through conventional clinical assessment.

The etiological component of the framework would concentrate on identifying potential underlying factors that are related to pica such as nutritional and environmental factors. Human evidence suggests that there are significant iron and pica relationships, and iron-related biomarkers, which may also be altered, as well as zinc status that may give some extra nutritional information[27]. Additionally, biomarkers related to exposure like blood lead may become clinically relevant for certain phenotypes like geophagia. The AI system may thus be used to combine ferritin, hemoglobin, MCV, RDW, serum iron, transferrin saturation, zinc, and clinically indicated toxicological measurements with patient characteristics and behavioral information. This would enable the model to differentiate potentially different etiological profiles from all forms of pica, rather than considering all pica as being biologically alike[28].

The pathophysiological part would be dedicated to the discovery of biological patterns and likely clinical implications related to pica. For instance, low ferritin, low MCV, high RDW and low hemoglobin may suggest an iron-deficiency-related phenotype, while blood lead concentration in the elevated range combined with geophagia may suggest physiological risk from lead exposure. Longitudinal AI could also be used to review changes in biomarkers over time and to see how well the abnormalities are being helped by the treatment. The outcomes of clinical events (e.g., gastrointestinal, continued abnormal nutrition, toxic element exposure, frequent healthcare visits) may be integrated into models that can be used to predict pica-related side effects and treatment efficacy[29].

Table 1: Summary of AI, Machine Learning, and Multimodality Studies Relevant to Clinical Risk Assessment[30]

Author(s) & Year	Study Focus	Methodology/Model	Key Findings
Pușcaș et al. (2025)[31]	Nasopharyngeal carcinoma prognosis	Radiomics + deep learning	Improved prognostic evaluation through quantitative imaging features and AI-based pattern recognition.
Oikonomou et al. (2026)[32]	Aortic stenosis assessment	AI-enabled echocardiography	Supported multimodality imaging and more efficient clinical assessment.
Kwiatkowska-Miernik et al. (2024)[33]	High-grade glioma progression	Machine learning	Demonstrated potential for predicting progression-free survival and individualized risk assessment.
Sinigiani (2026)[34]	Cardiac amyloidosis	Multimodality imaging	Highlighted the value of combining imaging modalities for diagnosis and risk stratification.
Sclafani et al. (2026)[35]	Cardiac amyloidosis	Advanced multimodality imaging	Supported early detection, risk stratification, and treatment-response monitoring.

Importantly, this proposed framework should be a clinical decision support system and not a standalone diagnostic tool. Future studies should aim to create large prospective human only datasets with standardized measures of pica phenotyping and longitudinal biomarkers measurements, which should be externally and prospectively validated with explainable AI models. This might provide a clinically acceptable framework for earlier identification, risk assessment and tailored management of pica in an understandable way, without losing monitoring and supervision.

5. DISCUSSION

This is a critical interpretation of human evidence on pica, etiological and pathophysiological biomarkers, and the potential of multimodal artificial intelligence (AI) and machine learning (ML) for predictive risk stratification, early detection and clinical management. The available evidence suggests that pica is a clinically heterogeneous disorder and is considered to be a particularly associated with iron deficiency, anemia, changes in hematological parameters, changes in zinc status and, in certain forms (e.g. geophagia), exposure to potentially toxic elements[36]. Human research also indicates that composite measures of two or more biomarkers might be more informative than any single measure. Meanwhile, opportunities exist for incorporating clinical, behavioral, laboratory, nutritional, toxicological, and electronic health-record data with the help of AI and natural language processing (NLP). Research developments in pica are still limited, however, there is evidence from related fields like iron-deficiency prediction, anemia prediction, and eating-disorder detection that can provide methodological support for pica-specific AI development but not direct evidence for the validation of pica-specific AI systems.

5.1 Interpretation and Analysis of Current Findings

The results suggest that pica is a multi-dimensional clinical disorder with nutritional, hematological, behavioral, developmental and environmental dimensions. Iron Deficiency and anemia have been suggested as important biological correlates of pica as evidenced from human evidence. Of the 262 adults (nonpregnant) with ID or IDA, about 45% reported pica, and those with pica had lower levels of hemoglobin, MCV, RDW, platelet count, and ferritin[37]. Human meta-analytic evidence has also shown a correlation between pica and anemia, and there was a significant depletion of plasma zinc, hemoglobin and hematocrit. The results indicate that there is a possible connection between pica and a general psychobiological profile of behavior. Human investigations of geophagia also provide evidence that this ingested material may have a clinical risk, often due to toxic-element exposure. As such, the behavioral phenotype as well as its biological consequences should be taken into account in pica assessment.

5.2 Significance and Implications of the Findings

The findings have important implications for developing predictive and personalized approaches to pica. Demographic data, behavioral data, hematological parameters, nutritional parameters, toxicological parameters, and clinical data including clinical text could all be combined in a multimodal AI to uncover combinations of risk factors that may not be identified through traditional assessment. For instance, low ferritin levels, decreased MCV, elevated RDW, and clinic symptoms of unusual cravings may be used as criteria for screening for pica, and symptoms of geophagia and anemia with elevated blood lead levels may be used for further toxicological evaluation. Similarly, human AI research in similar conditions indicates that there may be early predictive signals in the longitudinal laboratory data, and NLP can identify behavioral data from clinical data[38]. These methods may therefore help to recognize and monitor pica from a very young age onward, but are not yet validated pica-specific clinical tools.

5.3 Research Gaps and Limitations

There are some key caveats to the existing evidence. The main challenge is the lack of AI datasets and trusted predictive models specific to pica. Many studies have been conducted in computational laboratories specifically on similar disorders, like iron-deficiency, anemia, and other eating disorders, so their performance cannot be directly applied to pica. Biomarkers like anemia, low ferritin or changes in the RCIs are also non-specific and can be caused by many other medical conditions[39]. Also, clinical documentation can sometimes be incomplete or inconsistent, and this can impact the identification of pica-related behaviors using NLP. There may be additional differences between populations in age, pregnancy, developmental status, geographical environment, cultural practices and substance type that can also affect model performance. Last, black-box systems for AI can be hard to interpret for clinicians, so it's important that AI approaches are explainable and clinically interpretable.

5.4 Future Research Directions

Further studies should focus on large scale, prospective, geographically and demographically diverse human cohorts with standardized pica phenotyping and longitudinal biomarker measurements. Such data ought to incorporate behavioral traits, demographic and clinical data, hematological parameters, iron-related indicators, zinc status, clinically-relevant toxicological measures, and data from electronic health records. Longitudinal studies would be useful to see if biomarker abnormalities occur before the onset of pica, and if so, whether they increase as the severity of the pica increases and if treated, if they decrease after treatment. Further AI models should include explainable AI, external validation, culturally responsive modeling, and usage in future clinical evaluation[40]. NLP and laboratory and behaviour information could also enhance the identification of pica not recorded in structured information. The proposed system is not a stand-alone diagnostic system, but rather assists a clinician in making decisions about whether a patient is afflicted or not.

6. CONCLUSION

The present study demonstrates that a clinical syndrome of pica is a multifaceted and underrecognized condition linked to nutrition, hematological, behavioral, and environmental issues. Human studies have shown that iron deficiency, anemia, decreased ferritin, changes in hematological parameters, and decreased zinc levels are significant contributors to pica, and that certain types of pica behaviour like geophagia may also be related to exposure to toxic elements. The findings indicate that using these etiological and pathophysiological biomarkers, combined with clinical, behavioral, toxicological, and electronic health-record data, and analyzed using multimodal artificial intelligence and machine learning, may enhance risk stratification, early detection, and individualization of clinical management. But, there is limited research on pica using AI techniques, and current data on similar disorders cannot be viewed as a direct test of pica prediction models. Thus, future studies should target larger and more diverse human-based data sets, standardized phenotyping of pica, longitudinal evaluation of biomarkers, explainable AI, external validation and prospective clinical evaluation. Overall, multimodal AI has the potential to be a valuable clinical decision support tool for the diagnosis and treatment of pica and should be used in conjunction with, not instead of, clinical assessment.

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