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Prevalence and Aetiological Spectrum of Transaminitis among Patients with Non-Viral Hepatitis in a Rural Tertiary Hospital in Southern Nigeria

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Abstract:
Non-viral hepatitis remains a significant health concern in rural populations, where exposure to hepatotoxic substances is common, and healthcare resources are often limited. This study examined the aetiological distribution and associated transaminase patterns among 100 patients diagnosed with non-viral hepatitis in a rural Nigerian setting. Diagnoses were grouped into seven clinical categories: alcoholic hepatitis (20%), herbal toxicity (20%), drug-induced liver injury (15%), aflatoxin exposure (15%), autoimmune hepatitis (10%), parasitic infection (10%), and protein deficiency (10%). Alanine aminotransferase (ALT) levels were more frequently reduced than elevated. Protein deficiency (20%) and DILI (17%) were the leading causes of reduced ALT, whereas elevated ALT was more associated with DILI (10%) and autoimmune hepatitis (4%). A significant inverse correlation was observed between aetiology and ALT levels ($\tau_\beta = -0.337$, $p = 0.003$). Aspartate aminotransferase (AST) was predominantly elevated across most aetiologies. The highest elevations were seen in alcoholic hepatitis (20%), DILI (20%), herbal toxicity (15%), and aflatoxin exposure (15%). A stronger inverse correlation was found between AST levels and aetiology ($\tau_\beta = -0.477$, $p < 0.001$), suggesting AST may be more sensitive to certain toxic and inflammatory liver insults. These findings show the diagnostic utility of transaminase patterns in non-viral liver disease and reveal the contribution of preventable causes in rural settings. However, clinicians must apply a multidimensional approach to liver function interpretation by integrating biochemical data with clinical signs to ensure accurate diagnosis and optimal patient care with public health interventions aimed at controlling alcohol use, unregulated herbal remedies, and unsafe drugs.

Keywords: Transaminitis, liver enzymes, alanine aminotransferase (ALT), aspartate aminotransferase (AST), Alcoholic Hepatitis, Herbal Toxicity, Drug-Induced Liver Injury (DILI)

Introduction:

Transaminitis refers to an abnormal elevation in serum liver transaminase enzymes, primarily alanine aminotransferase (ALT) and aspartate aminotransferase (AST), which are sensitive indicators of hepatocellular injury or inflammation. These enzymes are predominantly found in hepatocytes, and their leakage into the bloodstream typically reflects liver cell damage, although they may also be elevated in other systemic conditions (Navarro & Senior, 2006). Traditionally, the most widely recognised causes of transaminitis are viral hepatitides, specifically hepatitis A, B, and C, which continue to pose a significant public health burden worldwide, especially in low- and middle-income countries.

However, a growing body of evidence suggests that non-viral causes are increasingly contributing to liver enzyme abnormalities, particularly in developing nations such as Nigeria. Non-viral aetiologies of transaminitis encompass a broad spectrum of conditions, including non-alcoholic fatty liver disease (NAFLD), alcoholic liver disease, drug-induced liver injury (DILI), autoimmune hepatitis, aflatoxin exposure, protein-energy malnutrition, and hepatotoxicity from unregulated herbal remedies (Chalasani *et al.*, 2012; Okenwa *et al.*, 2023; Ofori-Asenso & Agyeman, 2016). NAFLD, for instance, is emerging as a major cause of

liver disease globally and is now recognised as the hepatic manifestation of metabolic syndrome, with increasing prevalence among individuals with obesity, diabetes, and dyslipidaemia (Nwokediuko, 2005; Ogbera &Azenabor, 2010). Similarly, herbal and traditional remedies, widely consumed in sub-Saharan Africa due to cultural beliefs and limited access to formal healthcare, are often hepatotoxic due to unregulated formulations and undisclosed ingredients. In many clinical settings across sub-Saharan Africa, including Nigeria, diagnostic protocols are often skewed towards identifying viral hepatitis, while non-viral causes of liver dysfunction remain under-recognised. This imbalance may delay accurate diagnosis, appropriate intervention, and epidemiological understanding of liver disease burdens in these regions. Moreover, many patients with elevated liver enzymes are treated empirically or inadequately investigated due to limited diagnostic infrastructure, inconsistent record-keeping, and poor follow-up systems in public healthcare facilities. Despite the clinical importance of identifying the underlying cause of transaminitis, especially in patients who test negative for common hepatotropic viruses, there remains a dearth of local data addressing the prevalence and aetiological spectrum of non-viral transaminitis in tertiary care centres. Existing studies have primarily focused on viral hepatitis seroprevalence, with minimal emphasis on biochemical and clinical patterns of non-viral liver injury (Paruk *et al*., 2019).

This study, therefore, aims to evaluate the prevalence, demographic distribution, and aetiological profile of transaminitis in patients who are seronegative for hepatitis A, B, and C, as seen at a tertiary hospital in southern Nigeria. By shedding light on the non-viral drivers of liver dysfunction in this setting, the findings are expected to enhance clinical awareness, promote early detection, and guide appropriate management strategies tailored to the local disease burden.

Methods:

Study Design

This retrospective cross-sectional study was conducted at the Department of Internal Medicine, Igbinedion University Teaching Hospital, in collaboration with the Department of Biochemistry, Igbinedion University, Okada, Nigeria. The study covered medical records from January 2023 to March 2025. Medical records of 100 adult patients who presented with abnormal liver function tests (LFTs) and tested negative for hepatitis A, B, and C were reviewed.

Inclusion criteria:

- Age ≥18 years
- Abnormal alanine aminotransferase (ALT) and/or aspartate aminotransferase (AST) levels
- Seronegative for hepatitis A, B, and C

Exclusion criteria:

- Age <18 years
- Positive viral hepatitis serology
- Incomplete LFT records

Data Collection

Demographic data, clinical presentation, risk factors (such as alcohol intake and drug history), and final diagnosis were extracted from hospital records using a standardised data abstraction form. For analytical purposes, final diagnoses were categorised into clinically relevant aetiological groups, including alcoholic hepatitis, drug-induced liver injury (DILI), autoimmune hepatitis, aflatoxin exposure, parasitic infection, protein deficiency, and herbal toxicity. This classification was done jointly by the Medical Officer and reviewed by a Chief Consultant in collaboration with the Department of Biochemistry to ensure consistency in diagnostic grouping.

Biochemical Analysis

Serum ALT and AST levels were determined in the hospital's laboratory using an automated Roche Cobas® c111 analyser, following the International Federation of Clinical Chemistry (IFCC) standardised enzymatic colorimetric method, which measures enzyme activity at 37°C with optimised substrate concentrations for precision.

The normal reference ranges used were based on IFCC recommendations (Schumann *et al*., 2002):

- ALT (Alanine aminotransferase): 7–56 U/L
- AST (Aspartate aminotransferase): 5–40 U/L

These values were consistent with those adopted by the World Health Organization (WHO) and IFCC collaborative protocols, as well as those referenced in the instrument manufacturer's manual (Roche Diagnostics, 2009; World health Organization, 2017).

Transaminitis was defined as ALT and/or AST elevation ≥1.5 times the upper limit of normal (ULN), in line with commonly accepted clinical thresholds for hepatocellular injury severity classification.

Statistical Analysis

Data were analysed using IBM SPSS Statistics version 26. Descriptive statistics were used to summarise the data, and results were expressed as means, frequencies, and percentages.

This sample size of 100 was deemed sufficient based on similar published retrospective studies in Nigeria investigating transaminitis and non-viral hepatic causes (Adekanle *et al.*, 2020).

Ethical Approval

Ethical approval for this study was obtained from the Health Research Ethics Committee (HREC) of Igbinedion University Teaching Hospital (IUTH), Okada, Edo State, Nigeria, with protocol number IUTH/R.24/VOL.I/156. Patient confidentiality was maintained by anonymising all data, and the study adhered to the ethical principles outlined in the Declaration of Helsinki for research involving human subjects (World Medical Association, 2013).

RESULTS

Aetiologies of Liver Injury in Non-Viral Hepatitis Patients

Out of the 100 patients included in the study, the most common identified causes of non-viral hepatitis were alcoholic hepatitis and herbal toxicity, each accounting for 20% of cases. This was followed by aflatoxin exposure and drug-induced liver injury (DILI), which each constituted 15% of the study population. Autoimmune hepatitis, parasitic infections, and protein deficiency were the least frequent causes, each contributing 10% to the overall distribution. This distribution highlights the significant burden of modifiable or preventable aetiologies, such as alcohol use and herbal medication use in non-viral hepatic dysfunction within the study setting.

Table 1: Aetiologies of Liver Injury in Non-Viral Hepatitis Patients

AETIOLOGY	FREQUENCY (N)	PERCENT (%)
Aflatoxin Exposure	15.0	15.0
Alcoholic Hepatitis	20.0	20.0
Autoimmune Hepatitis	10.0	10.0
Drug-Induced Liver Injury	15.0	15.0
Herbal Toxicity	20.0	20.0
Parasitic Infection	10.0	10.0
Protein Deficiency	10.0	10.0
Total	100.0	100.0

Relationship between ALT and Aetiologies of Liver Injury in Non-Viral Hepatitis Patients

The clustered bar chart in Figure 1 illustrates the distribution of different aetiologies of liver injury in relation to ALT (Alanine Aminotransferase) levels, categorised as either elevated or reduced, among 100 patients. A significant association was observed between aetiology and ALT levels ($\chi^2 = 56.574$, $p < 0.001$), with a negative correlation noted (Kendall's $\tau = -0.337$, $p = 0.003$).

Overall, reduced ALT levels were more prevalent than elevated levels across nearly all aetiological categories. The most prominent finding is that protein deficiency accounted for the highest number of cases with reduced ALT, representing 20 patients (20%). This was followed by drug-induced liver injury (17 patients; 17%) and herbal toxicity (15 patients; 15%) in the reduced ALT group.

In contrast, elevated ALT levels were most commonly observed in cases of drug-induced liver injury (10 patients; 10%) and autoimmune hepatitis (4 patients; 4%). Other aetiologies such as aflatoxin exposure, alcoholic hepatitis, and parasitic infection each accounted for 3%–4% of the elevated ALT cases.

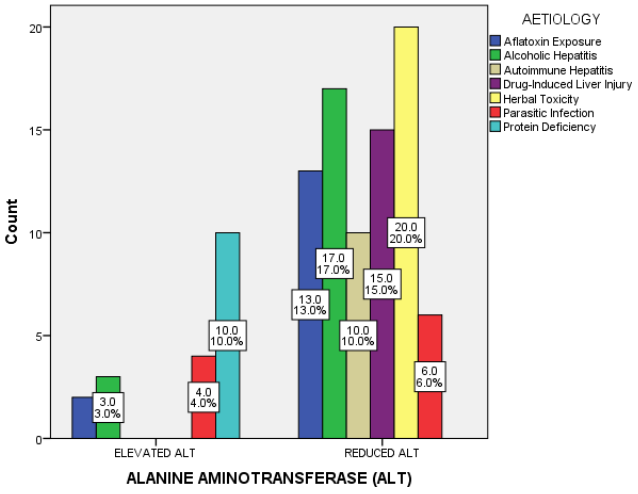

Figure 1: Relationship between ALT and Aetiologies of Liver Injury in Non-Viral Hepatitis Patients (elevated ALT >56U/L, reduced ALT <7U/L)

Relationship between AST and Aetiologies of Liver Injury in Non-Viral Hepatitis Patients

The clustered bar chart in Figure 2 illustrates the distribution of elevated and reduced Aspartate Aminotransferase (AST) levels across various aetiologies among 100 patients. A significant association was observed between aetiology and AST levels ($\chi^2 =$

61.000, $p < 0.001$). Also, a statistically significant negative correlation was found between AST levels and aetiology (Kendall's tau-b = –0.477, $p < 0.001$), suggesting that specific aetiologies are associated with a higher likelihood of AST elevation.

A majority of the cases showed elevated AST levels, particularly in patients diagnosed with alcoholic hepatitis (20%), drug-induced liver injury (DILI) (20%), herbal toxicity (15%), aflatoxin exposure (15%), protein deficiency (9%), autoimmune hepatitis (10%). In contrast, reduced AST levels were far less common and were mostly observed in: protein deficiency (10%) and parasitic infection (1%)

This pattern suggests that AST elevation is more prominent in hepatocellular injury from toxic, infectious, or inflammatory causes, with alcoholic hepatitis, drug-induced liver injury, and herbal toxicity being the leading contributors in this sample. The predominance of elevated AST reinforces its role as a marker of liver injury in non-viral hepatic conditions.

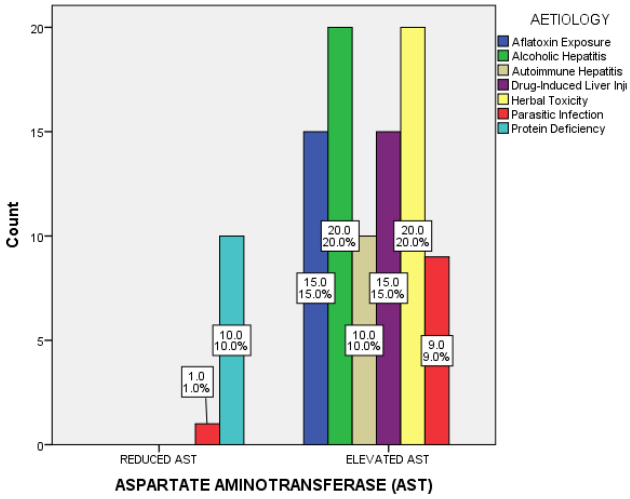

Figure 2: Relationship between AST and Aetiologies of Liver Injury in Non-Viral Hepatitis Patients

(elevated AST >40U/L, reduced AST <5U/L)

DISCUSSION

Aetiologies of Liver Injury in Non-Viral Hepatitis Patients

The observed distribution of non-viral hepatitis aetiologies in this study was seen as alcoholic hepatitis and herbal toxicity, each accounting for 20% of cases, followed by aflatoxin exposure and drug-induced liver injury (DILI) at 15% each, and autoimmune hepatitis, parasitic infections, and protein deficiency at 10% each.

The significant proportion of alcoholic hepatitis among patients in rural settings may be attributed to several factors, such as cultural practices and socioeconomic factors. In many rural communities, alcohol consumption is deeply ingrained in social and cultural practices. Locally brewed alcoholic beverages are often more accessible and affordable than regulated commercial products, leading to higher consumption rates. There is often limited awareness about the hepatotoxic effects of excessive alcohol intake. This lack of knowledge contributes to continued consumption despite the associated health risks. Also, rural areas frequently have inadequate healthcare infrastructure, making it challenging for individuals to receive education on the dangers of alcohol abuse and to access treatment for alcohol-related disorders. This is entirely devastating, as a study by Ndububa *et al.* highlighted alcohol consumption as an independent determinant in the progression of chronic liver disease in Nigeria, emphasising the role of alcohol in hepatic pathology within the region (Ndububa *et al*., 2005). The equal prevalence of herbal toxicity reflects the widespread use of traditional herbal medicines in rural areas (Auerbach *et al*., 2012). Due to limited access to conventional healthcare and poor health awareness deep-rooted in strong cultural beliefs and myths, rural populations often depend on traditional healers and herbal remedies for the treatment of various ailments. Herbal medicines are commonly perceived as natural and safe, leading to their unregulated use without consideration of potential hepatotoxic effects. Many herbal products are prepared without standardised dosages or quality control, increasing the risk of contamination with hepatotoxic substances. Research indicates that herbal medicine use is associated with significant liver fibrosis in both HIV-infected and uninfected individuals in sub-Saharan Africa. Additionally, the National Agency for Food and Drug Administration and Control (NAFDAC) in Nigeria has reported that high toxic content in herbal medicines can damage vital organs, including the liver (Auerbach *et al*., 2012; Punch Newspapers, 2020).

The notable incidence of aflatoxin-related hepatitis is likely due to the consumption of staple foods such as maize and groundnuts, which are susceptible to aflatoxin contamination, in rural areas. Inadequate storage conditions facilitate the growth of aflatoxin-producing fungi, increasing exposure risk. Furthermore, limited knowledge about aflatoxin contamination and insufficient food safety regulations contribute to ongoing exposure. Studies have shown that aflatoxin exposure is a significant risk factor for liver disease in regions where contaminated food storage is prevalent (Amadi & Orisakwe, 2018). The occurrence of DILI in rural

populations may stem from self-medication practices, which may be due to limited access to healthcare professionals; individuals often self-medicate with over-the-counter drugs, increasing the risk of hepatotoxicity. Likewise, the availability of counterfeit or substandard medications in rural markets can lead to liver injury, as well as inadequate monitoring of drug safety and adverse effects, which also contributes to the prevalence of DILI (Amadi & Orisakwe, 2018). A case series from a single centre reported that herb-induced liver injury, though less documented, is a growing problem, highlighting the need for careful assessment of herbal medicine use (Dağ *et al*., 2014).

Underdiagnosis of autoimmune hepatitis is common in rural areas due to limited access to specialised diagnostic tools and healthcare professionals, which may have been the reason for the low output in our findings. Also, while parasitic infections are prevalent, their progression to liver disease may be less frequent or underreported. Malnutrition, including protein deficiency, is prevalent in rural areas due to food insecurity, but its direct link to liver disease may not be well recognised or documented. Also, patients with protein-losing diseases like nephrotic syndrome or glomerulopathies in general might have the same presentation. The underreporting and lack of documentation of these conditions in rural settings contribute to their perceived lower prevalence (Amadi & Orisakwe, 2018).

Relationship between ALT and Aetiologies of Liver Injury in Non-Viral Hepatitis Patients

Transaminitis refers to elevated levels of liver enzymes, specifically ALT and aspartate aminotransferase (AST), indicating hepatocellular injury. ALT is primarily localised in the liver, making it a more specific marker for liver damage compared to AST, which is also found in other tissues such as the heart and muscles. Elevations in these enzymes typically suggest active liver inflammation or injury. However, the prevalence of reduced ALT levels in this study suggests alternative or additional pathophysiological mechanisms at play.

Severe protein malnutrition can lead to diminished synthesis of liver enzymes, including ALT. In protein-deficient states, the liver's capacity to produce these enzymes is compromised, leading to lower serum levels. This phenomenon has been observed in malnourished populations, where liver enzyme levels may not accurately reflect the extent of hepatic injury (Abulude *et al*., 2017). While DILI often presents with elevated liver enzymes, certain hepatotoxic drugs can cause mitochondrial dysfunction and hepatocellular necrosis without significant enzyme release, especially in chronic exposure scenarios. Additionally, some drugs may impair protein synthesis, leading to reduced enzyme production. The European Association for the Study of the Liver (EASL) notes that serum aminotransferase levels remain the mainstay for detecting and classifying liver damage in suspected DILI, but variations can occur depending on the drug and individual response (European Association for the Study of the Liver, 2019). Also, the use of hepatotoxic herbal remedies, common in certain regions, can lead to liver injury with variable enzyme patterns. Some herbal toxins may cause liver damage without significant enzyme elevation, particularly if the injury leads to impaired enzyme synthesis. This shows the importance of considering herbal medicine use in patients with liver dysfunction, even when standard liver enzymes are not elevated (Dağ *et al*., 2014). Furthermore, autoimmune hepatitis typically manifests with elevated transaminases due to ongoing immune-mediated hepatocellular inflammation. Persistent elevation of ALT is a hallmark of active disease and guides treatment decisions.

The predominance of reduced ALT levels in this study highlights the need for a careful interpretation of liver enzyme results. Relying solely on elevated transaminases to detect liver injury may lead to underdiagnosis, especially in conditions like protein deficiency or certain types of DILI and herbal toxicity. Comprehensive clinical assessment, including nutritional evaluation and detailed medication and herbal remedy histories, is essential for accurate diagnosis.

Relationship between AST and Aetiologies of Liver Injury Injury in Non-Viral Hepatitis Patients

In alcoholic hepatitis, AST levels often exceed ALT levels, typically with an AST/ALT ratio greater than 2:1. This pattern results from alcohol-induced mitochondrial injury and a relative deficiency of pyridoxal phosphate (vitamin B6), which affects ALT synthesis more than AST (Botros & Sikaris, 2013). Also, DILI can present with varying patterns of enzyme elevation, depending on the offending agent. Some drugs cause a hepatocellular injury pattern with predominant AST elevation. For instance, acetaminophen toxicity often leads to significant increases in AST levels, which is predominantly abused in rural communities (Francis & Navarro, 2024). In the same way, herbal-induced liver injury (HILI) is a growing concern, especially in regions with prevalent use of traditional medicines. Certain herbal compounds can cause hepatocellular damage, leading to elevated AST levels. The pattern of enzyme elevation in HILI varies, but significant AST increases

have been documented (Nunes *et al*., 2022). Furthermore, aflatoxins, produced by certain fungi, are potent hepatotoxins. Exposure can lead to acute liver injury characterised by elevated AST levels. Studies have shown that aflatoxin B1 exposure results in significant increases in AST, reflecting hepatocellular necrosis (Dhakal *et al*., 2023). Severe protein malnutrition can also impair liver function, leading to altered enzyme synthesis and release. While data are limited, some studies suggest that protein deficiency may result in elevated AST levels due to compromised hepatocellular integrity. Autoimmune hepatitis is characterised by immune-mediated hepatocellular inflammation, leading to elevated transaminases. Both AST and ALT levels are typically increased, but AST may be more prominently elevated in some cases (Linzay *et al*., 2023).

The predominance of elevated AST (aspartate aminotransferase) levels observed across various aetiologies in this study exposes the critical role of AST in the biochemical assessment of hepatic dysfunction, particularly in non-viral liver diseases. While both AST and ALT (alanine aminotransferase) are markers of hepatocellular injury, AST is less specific to the liver due to its presence in other tissues such as skeletal muscle, cardiac muscle, kidneys, and the brain. This broader tissue distribution means that elevated AST levels can arise from both hepatic and extrahepatic sources, including muscle trauma, myocardial infarction, and hemolysis (Botros & Sikaris, 2013). Therefore, clinicians are advised to interpret AST and ALT elevations alongside patient history, physical examination findings, imaging studies, and additional liver function parameters, such as alkaline phosphatase, bilirubin, albumin, and prothrombin time. For instance, in herbal toxicity or drug-induced liver injury (DILI), elevated AST might reflect active hepatocellular necrosis, but further confirmation via imaging (e.g., ultrasound or CT scan) and possibly liver biopsy may be required for definitive diagnosis and management.

Conclusion

This study unveils the biochemical and aetiological profiles of non-viral hepatitis among a rural population, with a particular focus on transaminase patterns. The findings reveal alcoholic hepatitis and herbal toxicity as the most common causes of liver dysfunction in this setting. This highlights the continued burden of modifiable and preventable risk factors in rural communities, where unregulated herbal medicine use, alcohol abuse, and nutritional deficiencies remain prevalent. Notably, elevated AST levels were more commonly observed than ALT across multiple aetiological categories. This suggests a predominance of hepatocellular injury, potentially complicated by systemic factors such as malnutrition, coexisting muscle injury, or chronic alcohol intake. The disproportionate elevation of AST over ALT, particularly in alcoholic hepatitis and drug-induced liver injury, exposes the relevance of AST as an important, though less liver-specific, marker of hepatic injury. Conversely, reduced transaminase levels, especially ALT, were seen in conditions like protein deficiency, possibly reflecting diminished hepatocyte synthetic function.

The study reinforces the importance of contextual interpretation of liver enzymes. AST and ALT levels should not be assessed in isolation but must be integrated with clinical, nutritional, and epidemiological data, especially in resource-limited environments.

Recommendations and Public Health Policies

1. **Community Education & Public Health Campaigns**: There is an urgent need for targeted health education programs in rural areas to raise awareness about the dangers of excessive alcohol use and unsupervised herbal medicine consumption.
2. **Regulation of Herbal Products**: Regulatory authorities should implement stricter controls on the production, sale, and advertisement of herbal remedies, with routine screening for hepatotoxic compounds.
3. **Routine Liver Function Screening**: In at-risk populations, particularly those with known exposure to hepatotoxins (e.g., alcohol, traditional herbs, aflatoxins), periodic liver enzyme screening should be promoted to allow for early detection of liver damage.
4. **Nutritional Interventions**: Since protein deficiency featured prominently in patients with reduced transaminase levels, community-level nutritional support and supplementation programs are warranted.
5. **Further Research**: Additional studies involving larger, multicentric rural populations with more extensive biochemical and histological assessments are recommended to validate and expand on these findings.
6. **Capacity Building for Rural Clinicians**: Training primary healthcare workers on the interpretation of transaminase levels, particularly in the context of rural liver disease, will enhance diagnostic accuracy and patient management.

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