

DETECTION OF HBc IgM ANTIBODIES AMONG FEBRILE PATIENTS ATTENDING A MODEL HEALTH CENTRE, RUMUEME, PORT HARCOURT, NIGERIA

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ABSTRACT: The primary laboratory technique for identifying hepatitis B virus (HBV) infection in feverish patients is hepatitis B surface antigen (HBsAg) testing. But depending only on HBsAg could miss acute or undetected HBV infections. The prevalence of hepatitis B core IgM antibody (anti-HBc IgM) in the South-South region of Nigeria is presently unknown. The purpose of this study was to determine the serological prevalence of anti-HBc IgM in patients with fever in Port Harcourt, Nigeria. Here, 92 febrile patients were tested for anti-HBc IgM using test kits in accordance with the manufacturer's instructions as part of a cross-sectional study. While 64.1% of participants tested negative, the overall prevalence of anti-HBc IgM was 35.9%. Higher prevalence rates were found in older age groups (44.7%), women (53.3%), single people (42.9%), people with postsecondary education (42.2%), and civil servants (47.4%). Nevertheless, anti-HBc IgM positivity was not statistically significantly predicted by any of the sociodemographic factors we evaluated. Crucially, the sole serological indicator of HBV infection in 33 (35.9%) febrile patients was anti-HBc IgM. This points to a potential recent or acute infection that HBsAg screening might overlook. The risk of HBV transmission to the general population from feverish individuals with isolated anti-HBc IgM positivity is highlighted by this finding. As a result, patients with fever in Port Harcourt frequently have anti-HBc IgM antibodies. For Nigerian patients with fever, we strongly advise routine screening for anti-HBc IgM. To the best of our knowledge, this study is the first to assess the prevalence of anti-HBc IgM in Nigeria's South-South region.

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1. INTRODUCTION

Hepatitis B virus (HBV) is a liver-targeting virus and a major cause of illness and death worldwide. It affects millions of people globally, with varying rates of infection in different regions (Aniche et al., 2022; Okonko et al., 2022). HBV leads to both acute and chronic liver disease and is highly common in areas like sub-Saharan Africa, Southeast Asia, and China (Inoue & Tanaka, 2016). In 2019, an estimated 296 million people had chronic HBV infection, with over 820,000 deaths related to HBV each year (WHO, 2021). Many infected individuals are undiagnosed, which shows the need for better detection methods (WHO, 2022).

HBV infection is the top cause of hepatocellular carcinoma (HCC), making up more than half of all cases globally. Infected individuals are 15 to 20 times more likely to develop HCC than those who are uninfected (Lavanchy, 2004; Parkin, 2006). While antiviral therapies can reduce viral replication, they do not eliminate covalently closed circular DNA (cccDNA), which maintains viral presence and disease progression (Gane, 2017). Therefore, early diagnosis is essential to reduce transmission, complications, and deaths related to HBV.

Diagnosing HBV involves several markers, such as hepatitis B surface antigen (HBsAg), hepatitis B e antigen (HBeAg), antibodies to surface antigen (anti-HBs), core antigen (anti-HBc IgG), envelope antigen (anti-HBe), and core IgM antibody (anti-HBc IgM). Each marker reflects different stages of infection (Kao, 2008; Towell & Cowie, 2012; Aniche et al., 2022). HBsAg shows up early in infection and is commonly used for screening; however, relying on HBsAg alone may miss acute infections during the "window period" or non-detectable HBV infections (Raimondo et al., 2019).

In Nigeria, HBsAg testing is the main laboratory method for diagnosing HBV (Jeremiah et al., 2011). This method may overlook infections in individuals who are HBsAg-negative but anti-HBc-positive. Anti-HBc IgM appears shortly after infection and is a reliable sign of acute or recent HBV infection. It is particularly useful for detecting infections during the window period (Kryger, 1985; Japhet et al., 2011). Thus, finding anti-HBc IgM improves diagnostic accuracy and enhances transfusion and public health safety.

Despite its important role in diagnosis and epidemiology, there is limited data on the prevalence of anti-HBc IgM in the South-South region of Nigeria. Febrile patients, who may have vague symptoms, could be a source of undetected HBV transmission. This study aims to determine the seroprevalence of anti-HBc IgM antibodies among febrile patients attending Model Health Centre, Rumueme, Port Harcourt, Rivers State, Nigeria.

2. MATERIALS AND METHODS

2.1 Study Area

The study area was the Model Health Centre, Rumueme, in Port Harcourt, Rivers State, Nigeria. A small communal settlement of the Ikwerre-speaking tribe of Rivers State, the people are known to be traders and other business activities done in its peaceful environment.

2.2 Study Design

This hospital-based cross-sectional study involves febrile patients at the Model Health Centre, Rumueme, in Port Harcourt, Rivers State, Nigeria.

2.3 Study Population

The targeted population constituted all febrile patients at the health centre to receive medical care. A total of 92 blood samples were collected from febrile patients who were included in the study.

2.4 Inclusion and Exclusion Criteria

The population included in this study comprised febrile patients who were at the Model Health Centre, Rumueme, in Port Harcourt, Rivers State, Nigeria and in which they gave their consent to participate in the study. Febrile patients who gave no consent were excluded from this study.

2.5 Sample Collection, Transport, Preparation & Storage

From the study population, 92 blood samples were collected from the febrile patients. Five millilitres (5 ml) of blood samples were aseptically collected from each patient into sterile EDTA tubes. The collected blood sample was carefully transported with an ice pack to the Virus & Genomics Research Unit of the Department of Microbiology, University of Port Harcourt. The blood samples were centrifuged in the laboratory, after which plasma samples were collected using a micropipette. After collection, these plasma samples were stored at -20°C until ready for use.

2.6 Serological Analysis

A commercial ELISA kit (Dia.Pro Diagnostic Bioprobes, Milan, Italy) was used to test plasma samples for hepatitis B core IgM antibody (anti-HBc IgM) in accordance with the manufacturer's instructions. Hepatitis B core antigen (HBcAg) antibodies can be found in human plasma or serum using the qualitative IgM-capture ELISA. IgM antibodies were collected on microplates coated with anti-human IgM, reacted with recombinant HBcAg conjugated with HRP, and then observed using a chromogenic substrate. Color intensity was inversely correlated with the concentration of anti-HBc IgM, and optical density was measured at 450 nm. Every run had both positive and negative controls. Sample-to-cutoff ratios (S/Co) were used to express the results; values $\geq$ cut-off were regarded as positive and values $<$ cut-off as negative.

2.7 Data analysis

Descriptive statistics were used to summarize the data, and the Statistical Package for Social Sciences (SPSS) version 25.0 was used for analysis. The chi-square test was used to evaluate associations between sociodemographic factors and the prevalence of HBc IgM, with a significance level of $p < 0.05$.

3. RESULTS AND DISCUSSION

3.1 Patients Characteristics

In this study, 92 febrile patients were tested for HBc IgM antibodies. Their age ranged between 20 – 63 years. Other socio-demographic data were as stratified in Table 1.

Table 1. Socio-demographic Characteristics of the studied Febrile Patient population

Characteristics	Categories	No. Tested	Percentage (%)
Age group (years)	20-35	54	58.7
	>36	38	41.3
Gender	Females	60	65.2
	Males	32	34.8
Marital status	Married	57	62.0
	Singles	35	38.0
Educational	No formal	8	8.7
	Primary	12	13.0
	Secondary	27	29.3
	Tertiary	45	48.9
Occupational status	Student	38	41.3
	Business/Trader	31	33.7
	Civil Servant	19	20.7
	Unemployed	4	4.3
Total		92	100.0

4.2 Overall Prevalence of HBc IgM Antibody

Of the 92 febrile patients tested for HBc IgM antibody, 33(35.0%) were positive and 59 (65.0%) were negative (Fig 1).

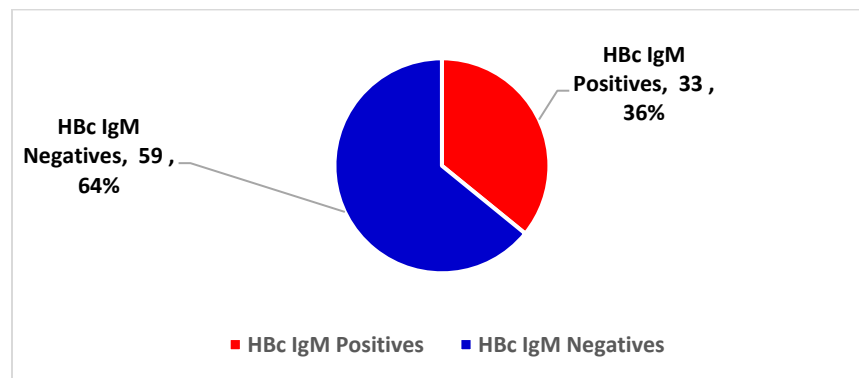


Fig. 1. Overall Prevalence of HBc IgM Antibody

4.3 Prevalence of HBc IgM Antibody with Age

This study indicates that the prevalence of HBc IgM antibody is higher in individuals within the age range of ≥ 36 years (44.7%) than in 20- 35 years (29.6%). Nevertheless, there was no significant relationship between the age ($p = 0.14$) groups and the prevalence of HBc IgM antibody (Fig. 2).

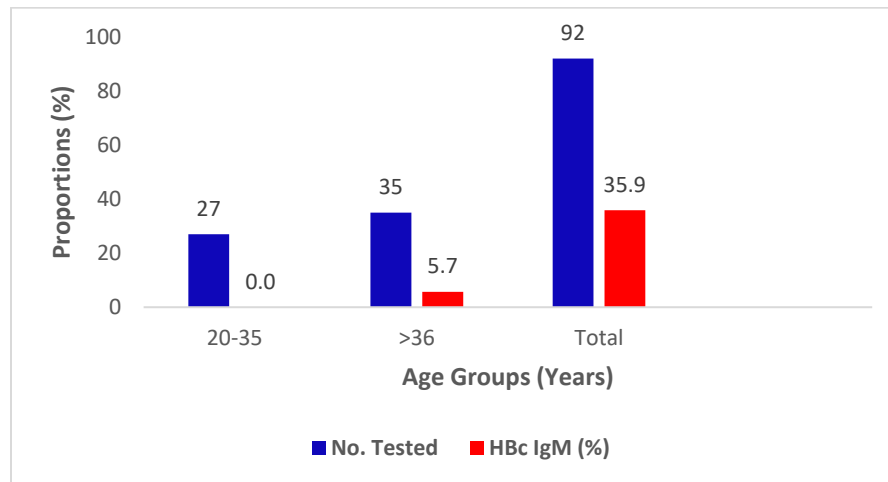


Fig. 2. Prevalence of HBc IgM Antibody with Age

4.4 Prevalence of HBc IgM Antibody with Gender

Fig. 3 shows the prevalence of HBc IgM antibody with gender. A higher prevalence of HBc IgM antibody occurred among females (53.3%) than males (31.3%). However, there was no relationship between gender ($p = 0.50$) and the prevalence of HBc IgM.

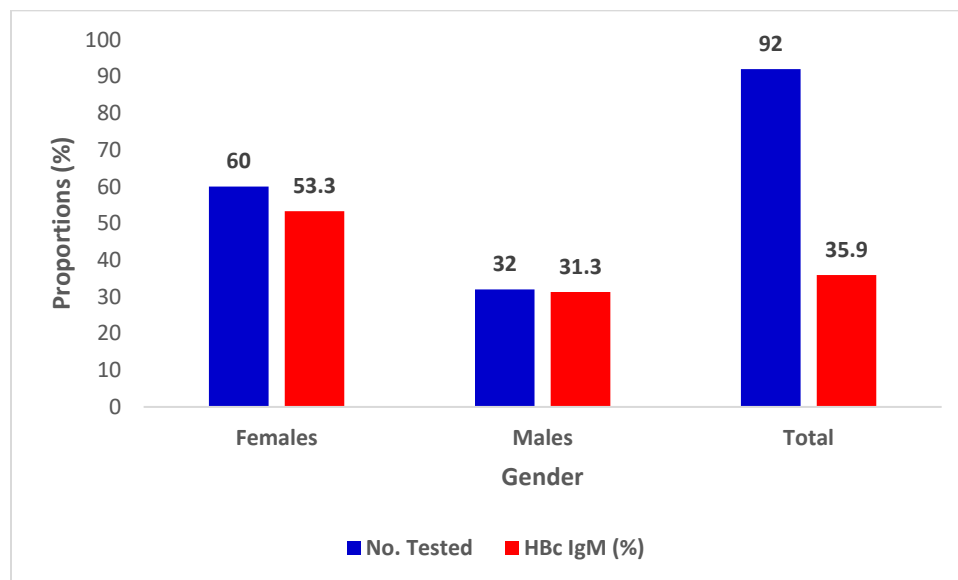


Fig. 3. Prevalence of HBc IgM Antibody with Gender

4.5 Prevalence of HBc IgM Antibody with Marital Status

From the result obtained, the prevalence of HBc IgM antibody occurred among singles (42.9%) than the married (31.6%). However, this difference was insignificant ($p = 0.27$), as in Fig. 4.

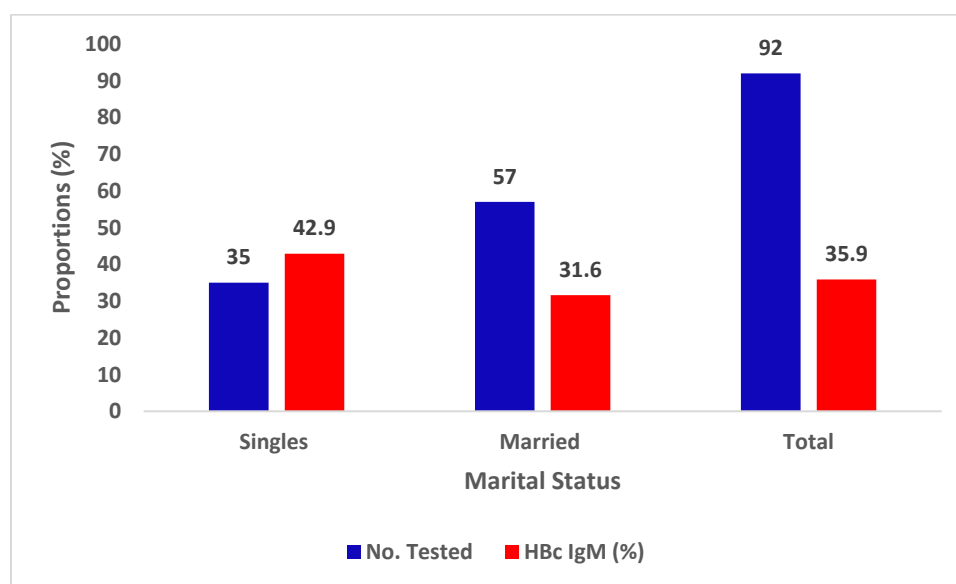


Fig. 4. Prevalence of HBc IgM Antibody with Marital Status

4.6 Prevalence of HBc IgM Antibody with Educational Status

The study indicates that the prevalence of HBc IgM antibody was higher in individuals with tertiary education (42.2%) than in those with other educational categories. Those with secondary education had 40.7%, followed by those without formal education (25.0%) and primary education (8.3%), this is as shown in Fig. 5. However, there was no relationship between educational status ($p = 0.14$) and prevalence of HBc IgM.

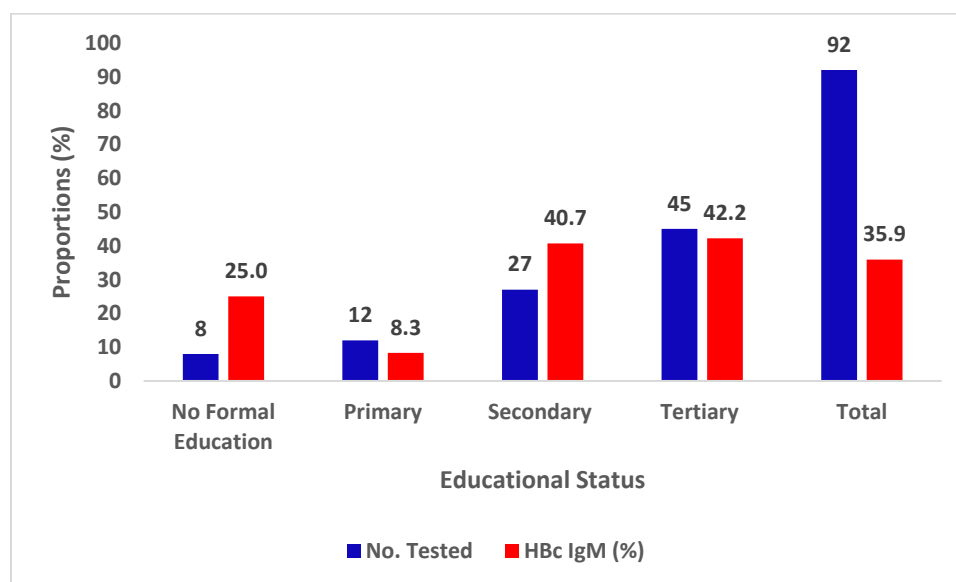


Fig. 5. Prevalence of HBc IgM Antibody with Educational Status

4.7 Prevalence of HBc IgM Antibody with Occupation

Out of these data, a higher prevalence of HBc IgM antibody occurred among civil servants (47.4%) than in other occupations, which were 42.1% for students, 25.8% for traders and 0.0% for the unemployed (Fig. 6). However, there was no relationship between occupation ($p = 0.15$) and prevalence of HBc IgM.

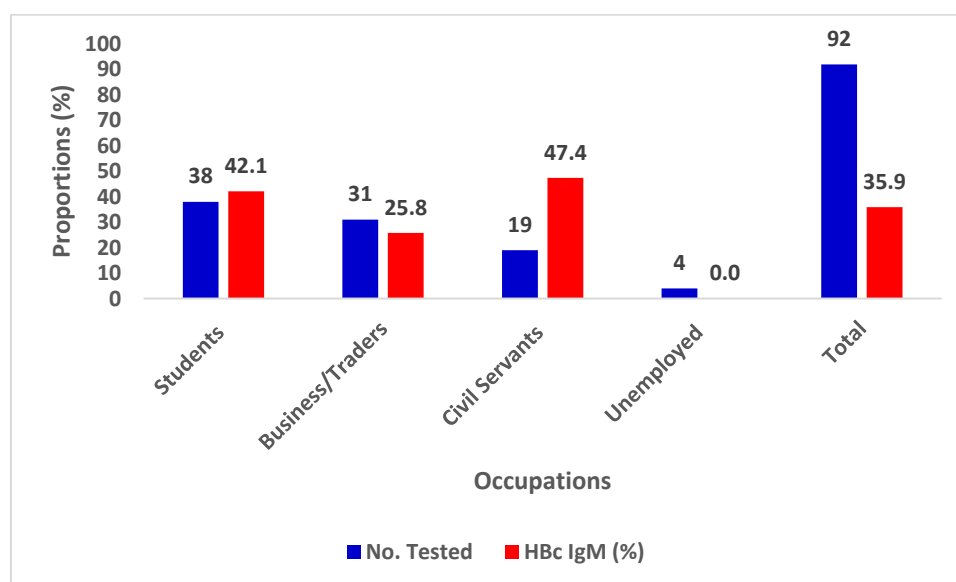


Fig. 6. Prevalence of HBc IgM Antibody with Occupation

4. DISCUSSION

Hepatitis B virus (HBV) infection, which mainly affects the liver and causes major complications like cirrhosis, fibrosis, and hepatocellular carcinoma (HCC), continues to be a significant global public health concern (WHO, 2022). Nearly one million liver-related deaths occur each year due to the virus, which is primarily spread by vertical transmission and contact with contaminated blood and bodily fluids (Mandiwana & Tshitenge, 2017). With over 18 million people currently infected and an estimated 75% of the population having been exposed at some point in their lives, Nigeria is a highly endemic country for HBV (Jombo et al., 2005; Berinyuy et al., 2019). Wide variations in HBV prevalence have been reported in earlier studies from Port Harcourt and other Nigerian cities, which can be attributed to variations in study settings, diagnostic techniques, and population groups.

Anti-HBc IgM antibodies were found to be highly prevalent (35.9%) among feverish patients in Port Harcourt, suggesting a recent or acute HBV infection that might not be picked up by routine HBsAg screening alone. The results corroborate previous findings that anti-HBc may be the only serological indicator of HBV infection, especially in occult infections or during the window period (Ogunfemi et al., 2017). The reported prevalence is higher than that found in Maiduguri, Ile-Ife, Enugu, and Southwestern Nigeria (Jeremiah et al., 2011; Salawu et al., 2011; Anaedobe et al., 2015; Aniche et al., 2022), but it is similar to reports from Ibadan (35.7%), Ilorin (32.5%), Iran (37.5%), and Benue State (38.2%) (Uemoto et al., 1998; Mbaawuaga et al., 2014; Ogunfemi et al., 2017; Fasola et al., 2022). These discrepancies most likely result from differences in screening methods, population characteristics, and regional HBV endemicity.

The high prevalence of anti-HBc IgM in febrile patients indicates significant exposure to HBV either recently or in the past. Anti-HBc antibodies highlight the possibility of HBV transmission from people who may be HBsAg-negative but still contagious because they can last a lifetime (Fasola et al., 2022). Lower endemicity, better vaccination rates, and increased public health awareness are the reasons for the comparatively lower prevalence rates (0.07–1.5%) reported in North America and Europe (Dhawan et al., 2008; Houareau & Offergeld, 2019).

Interestingly, 64.1% of participants had anti-HBc IgM-negative results, suggesting that they were susceptible to HBV infection. This identifies a sizable group of people who are at risk and would profit from focused immunization and more intensive public health initiatives. Although in smaller amounts, comparable susceptibility patterns have been documented in Enugu, Zimbabwe, and Southwestern Nigeria (Mzingwane & Mamvura, 2014; Ifeora et al., 2017; Aniche et al., 2022). From a public health perspective, it is noteworthy that 64.1% of the population were anti-HBc IgM negative, implying a large population at risk

of HBV infection. Therefore, vaccination and education programs for these individuals can be effective in controlling HBV transmission. However, a high anti-HBc IgM seroprevalence rate implies that febrile individuals can act as a reservoir for HBV infection, which necessitates routine HBV screening to prevent outbreaks.

Although a higher prevalence of anti-HBc IgM was found among persons aged >36 years, females, singles, those with tertiary education, and civil servants, none of the socio-demographic characteristics showed a statistically significant association with anti-HBc IgM positivity. These results are consistent with the findings of Japhet et al. (2011) and Fasola et al. (2022). These results differ from the findings of studies done in Ilorin and Enugu, where significant differences in anti-HBc IgM positivity were found with increasing age (Ogunfemi et al., 2017; Aniche et al., 2022). The increased prevalence of anti-HBc IgM with increasing age has been attributed to cumulative exposure during periods of increased HBV endemicity (Lim & Yoon, 2009; Roman et al., 2013).

The absence of significant associations with gender, marital status, education, and occupation suggests that HBV exposure in this population may be quite common and not driven by specific socio-demographic factors. However, the increased prevalence among civil servants and students could be a reflection of occupational mobility, social mixing, or healthcare exposure, as previously suggested (Okonko et al., 2010; Baye & Yohannes, 2007).

Overall, the prevalence of anti-HBc IgM in febrile patients emphasizes the limitation of solely depending on the HBsAg test for the diagnosis of HBV infection in Nigeria. The inclusion of anti-HBc IgM in the screening process, particularly in febrile patients, may be beneficial for the diagnosis of HBV infection. The diagnostic implications of this study are considerable. The sole use of HBsAg may result in underestimation of HBV infection, particularly in the window period or occult HBV infection. The use of anti-HBc IgM in the diagnostic algorithm for patients with fever may enhance early detection, prevent transmission, and guide interventions. The early detection of HBV infection is important for early clinical management and the prevention of chronic liver disease and HCC.

5. CONCLUSION

In summary, the observed prevalence of anti-HBc IgM in febrile patients in Port Harcourt, Nigeria, underscores a significant public health need and the rationale for extending HBV diagnostic approaches beyond HBsAg. The incorporation of anti-HBc IgM screening into vaccination initiatives and public health campaigns could have a profound impact on the control of HBV and overall health outcomes in Nigeria.

Compliance with ethical standards

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Disclosure of conflict of interest

The authors have declared that no competing interests exist.

Statement of ethical approval

All authors declare that all experiments have been examined and approved by the University of Port Harcourt Research Ethics committee. Therefore, the study is performed following the ethical standards laid down in the 1964 Declaration of Helsinki.

Statement of informed consent

"All authors declare that informed consent was obtained from all individual participants included in the study."

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