

**Original contribution**

Acidophil bodies in nonalcoholic steatohepatitis^{☆,☆☆}



**Matthew M. Yeh MD, PhD^{a,*}, Patricia Belt BS^b, Elizabeth M. Brunt MD^c,
Kris V. Kowdley MD^d, Laura A. Wilson ScM^b,
Linda Ferrell MD^e, for the Nonalcoholic Steatohepatitis Clinical Research Network**

^aDepartment of Pathology, University of Washington School of Medicine, Seattle, WA 98195

^bDepartment of Epidemiology, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD 21205

^cDepartment of Pathology and Immunology, Washington University School of Medicine, St. Louis, MO 63110

^dLiver Center, Swedish Medical Center, Seattle, WA 98104

^eDepartment of Pathology, University of California School of Medicine, San Francisco, San Francisco, CA, United States 94143

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Summary The significance of the quantity of acidophil bodies (AB) in nonalcoholic steatohepatitis (NASH) is not certain. We quantified AB in liver biopsies and examined the association with the diagnosis of NASH and other histologic features. We reviewed 157 liver biopsies from the NASH Clinical Research Network Database collected in 2006. One hundred twenty-seven biopsies were from adult patients. Diagnoses were 94 definite NASH, 40 borderline NASH, and 23 definitely not NASH. The total length and average width of the core biopsies were measured, and the biopsy areas were calculated (mm²). Total AB were counted, and mean AB count per mm² was calculated (AB/mm²) to derive acidophil body index (ABI). ABI was 0.04 (±0.08) in definite NASH and 0.02 (±0.05) in borderline/definitely not NASH groups combined ($P = .02$) in all 157 biopsies; similar findings were present in the 127 adult-only biopsies (0.04 ± 0.05 and 0.02 ± 0.05 , respectively; $P = .05$). In all 157 biopsies, increased ABI was associated with greater lobular inflammation ($P = .01$) and many ballooned hepatocytes ($P = .048$). There was a positive relationship between ABI and high nonalcoholic fatty liver disease activity scores, but this association was not statistically significant. There was no association between ABI and steatosis or fibrosis stage either in the entire cohorts or in the subset of adult patients. In conclusion, the density of AB is associated with lobular inflammation, ballooned hepatocytes, and the diagnosis of NASH in adult and pediatric liver biopsies, suggesting the implication of the apoptotic pathway in NASH-associated liver cell injury.

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* Corresponding author. Department of Pathology, University of Washington School of Medicine, 1959 NE Pacific St, NE140D, Box 356100, Seattle, WA, 98195.
E-mail address: myeh@u.washington.edu (M. M. Yeh).

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1. Introduction

Nonalcoholic fatty liver disease (NAFLD) has become a global epidemic in the 21st century, as it is the hepatic manifestation of the metabolic syndrome that is universally associated with the myriad of metabolic aberrations related to insulin resistance, in which type 2 diabetes, truncal obesity, dyslipidemia, hyperlipidemia and arterial hypertension are the best known features [1–3]. It is estimated that 20% to 30% of adults in the United States and Western Europe have excessive fat in the liver and that 10% of these individuals (2%–3% of adult population) may also meet current diagnostic criteria for the progressive disease nonalcoholic steatohepatitis (NASH) [4]. NASH may result in liver fibrosis and progress to cirrhosis, which may lead to liver-related death or hepatocellular carcinoma, or require liver transplantation [5]. The diagnosis of NASH continues to depend on histopathology. The diagnostic features of NASH center on the histologic constellation of steatosis, inflammation, and hepatocellular injury in the form of ballooning of hepatocytes. The clinical absence of significant alcohol use is required [6,7]. Among the histologic features, inflammation and hepatocyte ballooning reflect various injury cascades [1,8]. The morphologic identification of

ballooned hepatocytes may be difficult by routine stains and may depend on the pathologists' experience [6]. Because of the known damage to hepatocytes, immunohistochemistry for keratins 8 and 18 has been proposed for demonstrating this form of injury [9]. In addition, injury to hepatocytes may be present as other forms including spotty necrosis and apoptosis. For example, apoptotic bodies, also known as acidophil bodies (AB) (Fig. 1A and B), which are hepatocytes undergoing programmed cell death, are commonly seen in viral hepatitis. In fact, Saxena et al [10] have suggested that the density of apoptotic bodies can reliably distinguish early recurrent hepatitis C from acute cellular rejection in the early phase after orthotopic liver transplantation. Recent clinical and animal studies have suggested that apoptosis genes and related proteins are upregulated in NASH [11,12]. Caspase-3-generated fragment of cytokeratin (CK) 18, a marker for apoptosis, is also increased in individuals with NASH but not in individuals with steatosis only or borderline NASH [12].

Although apoptosis may be associated with liver injury in NASH, it is not certain if the quantity and density of AB are associated with the diagnosis of NASH. In this study, we quantified AB in liver biopsies and examined the association with the diagnosis of NASH and related histologic features.

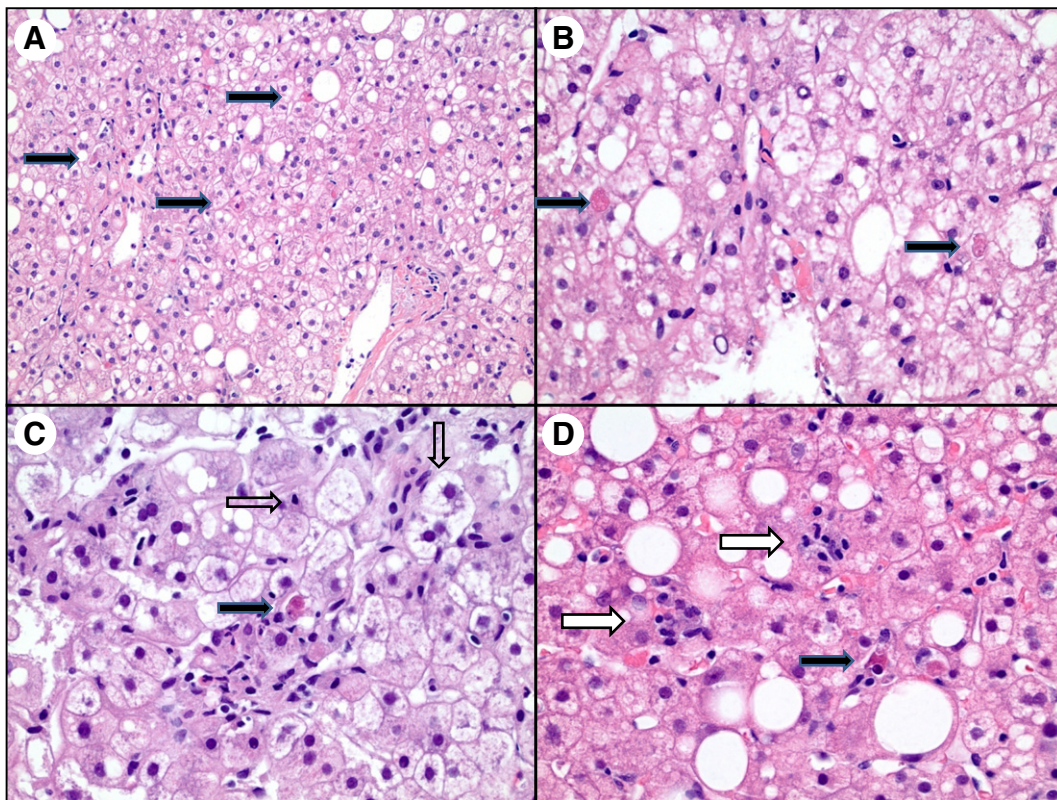


Fig. 1 AB (arrows) are present in the background of steatohepatitis (A, original magnification $\times 200$). Under higher magnification, AB (arrows) are characterized by eosinophilic and shrunken cytoplasm and pyknotic nuclei that may eventually disappear (B, $\times 400$). AB (black arrows) are commonly present with ballooned hepatocytes (C, blank arrows, $\times 400$) and lobular inflammatory infiltrates (D, white arrows, $\times 400$) that are composed of lymphocytes and Kupffer cells.

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