## Comment on: evaluating age and sex-specific rates of gall bladder disease in children with sickle cell disease

Ifra Eeman Ahmed<sup>1</sup> and Satesh  $\operatorname{Kumar}^2$ 

<sup>1</sup>Federal Medical and Dental College <sup>2</sup>Shaheed Mohtarma Benazir Bhutto Medical College

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**TITLE PAGETitle:** Comment on: evaluating age and sex-specific rates of gall bladder disease in children with sickle cell disease

**Article type:** Letter to the editor**Correspondence** : 1. Ifra Eeman Ahmed contact : 03335890003 Email : ifraeemanahmed786@gmail.com

Institution : Federal medical & dental college, Islamabad

Address: House#2,Street#15g,Sector A,Bahria Enclave,Islamabad

Co-author : 2. Satesh Kumar

Contact: +92-3325252902 Email:

Institute: Shaheed Mohtarma Benazir Bhutto Medical College Liyari, Karachi

Address: Parsa citi Garden east, Karachi

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To the editor,

The article by Agawu et al. "evaluating age and sex-specific rates of gall bladder disease in children with sickle cell disease" piqued our interest[1]. This study confirms that age, but not gender, is significantly associated with the incidence of GBD in paediatric patients with sickle cell disease. The large sample size of 13,745 individuals drawn from diverse geographic regions across the United States enhances the generalizability of the findings. It significantly adds to previously collected data analysing the incidence of GBD in children with SCD. However, we would like to add a few observations that do not diminish the study's validity.

In this study, the presence of the uridine diphosphate (UDP)-glucuronosyltransferase 1A (UGT1A) genotype cannot be determined. Children with the abnormal 7/7 UGT1A genotype had an average serum bilirubin concentration significantly higher than those with either the 6/6 or 6/7 genotype. The UGT1A promoter polymorphism is a significant nonglobin genetic modifier affecting bilirubin levels and symptomatic gallstone development in children with SCA[2].

Also, the relationship between SCD manifestation severity and glutathione S-transferase gene (GSTM1, GSTT1, and GSTP1) polymorphisms was not investigated. Several studies have reported that the GSTT1 null genotype results in the absence of functional protein, which may increase susceptibility to oxidative DNA damage and excessive ROS generation, resulting in an increased risk of SCD development and a predictor for the development of SCD complications [3]. Studies indicate a connection between blood transfusion and gallstones[4]. Although the status of transfusions during the study period was recorded, no information regarding the history of transfusions was collected or analysed. This prevents the researchers from establishing a correlation between blood transfusion and the occurrence of gallbladder disease in SCD-affected children. Due to the age-related increase in gallstone occurrence, it is estimated that 30% of SCD will have gallstones by the time they reach the age of 18. Thirteen-year-olds are the youngest SCD patients diagnosed with gallbladder calculus. There appears to be a substantial disparity between the prevalence of cholelithiasis in patients from Jamaica and North America and those from Africa. Variations in cholesterol and fibre intake may explain this disparity, but it's also possible that other factors (genetic or environmental) have a role. Cholecystectomy is the most common surgical operation in SCD patients, accounting for up to 40% of all surgical procedures due to the prevalence of cholelithiasis in SCD.[4,5]

## **References:**

1.Agawu A, Shults J, Smith-Whitley K, Feudtner C. Age- and sex-specific rates of gall bladder disease in children with sickle cell disease. Pediatr Blood Cancer. 2022;69(11):e29863. doi:10.1002/pbc.29863

2.Passon RG, Howard TA, Zimmerman SA, Schultz WH, Ware RE. Influence of bilirubin uridine diphosphateglucuronosyltransferase 1A promoter polymorphisms on serum bilirubin levels and cholelithiasis in children with sickle cell anemia. J Pediatr Hematol Oncol. 2001;23(7):448-451. doi:10.1097/00043426-200110000-00011

3.Shiba HF, El-Ghamrawy MK, Shaheen IA, Ali RA, Mousa SM. Glutathione S-transferase gene polymorphisms (GSTM1, GSTT1, and GSTP1) in Egyptian pediatric patients with sickle cell disease. Pediatr Dev Pathol. 2014;17(4):265-270. doi:10.2350/14-03-1452-OA.1

4.Inah GB, Ekanem EE. Sonographic Diagnosis and Clinical Correlates of Gallbladder Stones in Patients with Sickle Cell Disease in Calabar, Nigeria. Open Access Maced J Med Sci. 2019;7(1):68-72. Published 2019 Jan 12. doi:10.3889/oamjms.2019.015

5.Stender S, Frikke-Schmidt R, Nordestgaard BG, Tybjærg-Hansen A. Extreme bilirubin levels as a causal risk factor for symptomatic gallstone disease. JAMA Intern Med. 2013;173(13):1222-1228. doi:10.1001/jamainternmed.2013.6465