Open Access
Publish Free

http://jept.ir
doi 10.15171/jept.2015.03

Journal of Emergency Practice and Trauma
Volume 2, Issue 1, 2016, p. 7-10

Original Article

Identifying high and low serum-ascites albumin gradient in ascitic fluid by the point of care dipstick test

Leyli Asadabadi, Mohammad Mehdi Heyran, Amirhossein Mirafzal*

Department of Emergency Medicine, Kerman University of Medical Sciences, Kerman, Iran

Received: 7 May 2015
Accepted: 9 July 2015
Published online: 15 September 2015

***Corresponding author:** Amirhossein Mirafzal, Department of Emergency Medicine, Kerman University of Medical Sciences, Kerman, Iran.
Tel: +989121362984,
Email: a.mirafzal@yahoo.com, mirafzal@kmu.ac.ir

Competing interests: None.

Funding information: None.

Citation: Asadabadi L, Heyran MM, Mirafzal A. Identifying high and low serum-ascites albumin gradient in ascitic fluid by the point of care dipstick test. Journal of Emergency Practice and Trauma 2016; 2(1): 7-10. doi: 10.15171/jept.2015.03

Abstract

Objective: To evaluate the capability of ascitic fluid dipstick results for pH, glucose, and protein in order to predict a low serum-ascites albumin gradient (SAAG) at the bedside of the patient in the emergency department (ED).

Methods: This prospective cross-sectional study was conducted during one year in the ED of Afzalipour hospital in Kerman, Iran. All patients with diagnostic or therapeutic paracentesis of ascitic fluid were considered as eligible patients. Exclusion criteria included clinical suspicion for spontaneous bacterial peritonitis (SBP), any contraindications to paracentesis, and patients' refusal to participate in the study. Dipstick values were obtained at the bedside, and SAAG was calculated after the determination of serum and ascitic fluid albumin by laboratory. A low SAAG ascitic fluid was defined as the study outcome. We also used our study population as a test group to evaluate an equation proposed in one previous study: K = 0.012 Protein−0.012 Glucose−3.329 pH+23.498

Results: A total of 50 patients were enrolled in the study. Based on multivariate regression analysis, dipstick values for protein and glucose were independently predictive of a low SAAG ascitic fluid ($P=0.23$, OR = 1.04; and $P=0.001$, OR = 0.81, respectively). The formula proposed in one of the previous studies was tested by our data set, with sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) at 84%, 83%, 84%, and 80%, respectively.

Conclusion: Dipstick test of ascitic fluid for pH, glucose, and protein has an acceptable sensitivity and specificity as a point of care test, but it cannot be recommended as a substitute for SAAG determination based on the current findings.

Keywords: Serum-asictes albumin gradient, Ascitic fluid, Dipstick test

Introduction

Sending ascitic fluid to the laboratory for analysis is frequently done in healthcare facilities. Although the cause of ascites may seem clinically obvious in many cases, but an exact diagnosis needs to be clarified by analyzing this fluid. The recommended first-line laboratory test for ascitic fluid is serum-ascites albumin gradient (SAAG), after which other tests are performed based on the results (1). Formerly, a low SAAG ascetic fluid was termed "exudative ascitis" and a high SAAG was termed "transudative ascitis" (2), but these terminologies were brought into question later and most authors preferred to use "low SAAG" and "high SAAG" instead of "exudates" and "transudates" (3,4). Based on ascitic fluid SAAG, a spectrum of differential diagnoses can be considered for further workup. In the case of low SAAG, differential diagnoses may include tuberculous peritonitis-induced ascites, malignancy-induced ascites (for instance, peritoneal carcinomatosis, gastric and ovarian cancer metastases), pancreatic ascites, renal ascites, biliary ascites, bacterial peritonitis, and serositis-induced ascites. On the other hand, high gradient ascites are uncomplicated cirrhosis-induced ascites, heart-failure-induced ascites, those induced by extensive liver metastases and other circumstances such as fulminant hepatic failure (5-7).

Point of care examination of the ascitic fluid by urinary dipstick was studied extensively by some investigators, but their focus was mainly maintained on detecting infections (namely, spontaneous bacterial peritonitis [SBP]) rather than differentiating between high and low values of SAAG (8-11). Some studies found acceptable accuracy for dipstick tests (leukocyte esterase) to detect peritonitis in ascitic fluid (12,13), whereas other studies (including the largest one) concluded that dipstick test does not have sufficient sensitivity to detect SBP (14,15). The focus of previous studies on dipstick tests for ascetic fluid was perhaps due to the fact that a rapid diagnosis of SBP would be useful in initiating a suitable empirical antibiotic awaiting the

results of culture. The differentiation of low SAAG from high SAAG ascitic fluid by a point of care test in the emergency department (ED) may not have such a treatment effect, but undoubtedly, it can omit the first step of SAAG determination that is recommended today if it proves to be reliable enough.

In the present study, we evaluated the association between dipstick values of pH, protein, and glucose with a low SAAG (exudative) fluid and their predictive value for this outcome. We also assessed the reliability of an equation introduced by Heidari et al (16) to differentiate between low SAAG and high SAAG fluids by our data set.

Methods

This was a cross-sectional study performed prospectively on patients with ascites admitted to the ED of Afzalipour hospital. Afzalipour hospital is a referral center for Internal Medicine, Pediatrics, and Obstetrics/Gynecology located in Kerman, a large city with a population of nearly 1 million in the southeast of Iran. The Internal Medicine ED has an annual census of approximately 30000 patient encounters.

All patients admitted to Internal Medicine ED in which an abdominal diagnostic (e.g. in new onset ascites) or therapeutic (e.g. tense ascites with respiratory distress) paracentesis were performed by the managing team between February 15, 2014 and February 14, 2015 were considered as eligible patients. Exclusion criteria were defined as clinical suspicion for SBP (e.g. fever or abdominal tenderness), any contraindications to paracentesis (e.g. severe coagulopathy), and patients' refusal to participate in the study. All patients read (or made a companion read for them) and signed an informed consent form.

Abdominal paracentesis in Afzalipour ED is performed by residents of emergency medicine (post-graduate year (PGY) 1 or 2). The decision for paracentesis is made by the attending physician of emergency medicine. When the volume of ascitic fluid is estimated to be low, paracentesis is performed after marking the best site for the procedure by a resident of radiology. Paracentesis is mostly done from left or right lower quadrant sites rather than midline in our center.

After a patient was enrolled in the study, paracentesis was performed by one of the members of the managing team in the presence of our researcher; the researcher was a resident of emergency medicine (PGY 3) with the responsibility of performing the dipstick test and recording all available variables in a predesigned standardized sheet. A 5-10 ml specimen was taken by the researcher to perform dipstick tests according to the instructions of the producing company, and 10 ml specimens in other appropriate tubes were immediately sent to the laboratory for cell count and cytology, biochemistry (albumin and total protein), and culture. A simultaneous blood sample for albumin was also taken for each patient to measure serum albumin level. As the results of our standard variable (SAAG) were not available immediately, blinding of the researcher was not considered at the bedside in this study. All of this process was performed under the supervision of an attending physician of emergency medicine (a single person), and all dipstick readings were done by both the researcher and the supervisor. Inter-observer agreement was calculated to be 90% (excellent agreement), and the remaining cases of disagreement were resolved by consensus with a third party.

Dipstick strips used in this study were urinary dipsticks (KimiaPajoohan, IRAN) with cut points of 30, 100, and 500 md/dL for protein; 50, 100, 250, and 500 mg/dL for glucose, and 5, 6, 6.5, 7, 8, and 9 for pH.

For each patient, SAAG was calculated by subtracting ascitic fluid albumin from blood albumin level; both were measured in the laboratory of Afzalipour hospital by an autoanalyzer (Selectra 2). SAAG was defined as our gold standard and set as the definition of high SAAG (>1.1 mg/dL or formerly transudate) and low SAAG (<1.1 mg/L or formerly exudate). We chose a low SAAG ascitic fluid as the study outcome. Dipstick values for blood, pH, glucose, and protein were read and recorded. For protein and glucose, the cut points equivalent to the color of dipstick were recorded as mg/dL.

For univariate analysis, continuous data were analyzed using the *t* test if the data were normally distributed (according to the Kolmogorov-Smirnov, Shapiro and Levene test); otherwise, the adjusted *t* test was used. Categorical data were compared using Pearson $\chi 2$ test. A *P* value less than 0.05 was considered to be statistically significant. In multivariable model, we entered all variables with a potential to predict the outcome according to our clinical experience. The multivariable analysis was performed by constructing a logistic regression model according to forward Wald method. Independent associations were reported according to the model. In the final step, we put the whole group as the test group for evaluation of the model introduced by Heidari et al (16), which presented the following equation to evaluate its accuracy:

K = 0.012 Protein−0.012 Glucose−3.329 pH+23.498

Results

A total of 50 patients were enrolled in the study. Twenty-nine (58%) were male and 21 (42%) were female. The mean (SD) age was 53.6 (1.8), with the minimum of 18 and the maximum of 90 years. Twenty-nine patients (58%) had high SAAG and 21 patients (42%) had low SAAG ascitic fluids.

Table 1 shows the characteristics of ascitic fluids in each group. The dipstick values for glucose, protein, and pH were all significantly different between the 2 groups ($P<0.001$, $P=0.002$, and $P<0.001$, respectively). The mean laboratory measured value for pH was also significantly lower in the low SAAG group, whereas laboratory measured values for glucose and protein did not show a significant difference between two groups.

The dipstick values for pH, protein, and glucose were put in a multivariate regression model. Since the values for glucose and protein were 3 digit variables, they were divided by 10 to magnify their true association with the SAAG group. There were dipstick protein and dipstick glucose levels remained in the final step ($P=0.23$, OR = 1.04; and $P=0.001$, OR = 0.81, respectively). Dipstick pH was not associated with the outcome in this analysis ($P=0.36$). There was a 95% greater probability of obtaining a low SAAG ascitic fluid in a 50 mg/dL (1+) dipstick glucose level relative to a 100 mg/dL (2+) level. Other associations would also be calculable according to this analysis.

In the final step of the analysis, we entered our data set into the equation found by Heidari et al (16) to determine its accuracy (see Methods/Statistical analysis). We obtained a sensitivity of 84%, specificity of 83%, positive predictive value (PPV) of 84%, and negative predictive value (NPV) of 80% for this equation to predict a low SAAG (formerly exudative) ascitic fluid.

Discussion

Determining a low or a high SAAG ascitic fluid in the bedside can lead to ordering further tests in the ED, preventing a second fluid tap and reducing the admission time of patients. After taking the study of Heidari et al (16) into consideration, in which the accuracy of dipstick test to differentiate between high and low SAAG was evaluated, we were inspired to perform this study with the same method in a different setting and with different population to assess the congruency of the results. In the study of Heidari et al (16), an independent association was found between dipstick values of ascitic fluid (pH, protein, and glucose) with low SAAG (they used the term "exudative," which we prefer not to use it) ascitic fluid. They proposed an equation based on the logistic regression analysis and tested its sensitivity, specificity, PPV, and NPV by a subset of their study population not included in the analysis (93.8%, 94.4%, 89.5%, and 96.9%, respectively). These high values tempted us to assess this formula by a different data set.

In our study, we found independent associations between ascitic fluid dipstick values of protein and glucose with low SAAG ascitic fluid. PH did not show an independent association, although it was correlated with a low SAAG fluid in the univariate analysis. This was an indicator to the fact that our data would not yield a sensitivity, specificity, PPV, and NPV as high as those found by Heidari et al (16). After entering values in the formula, we obtained these values as stated in the results section. These parameters, although not as high as those found in the previous study, are still in an acceptable range for a point of care diagnostic test. However, the gold standard test (SAAG determination by laboratory) is still recommended to be done absolutely by our findings. Some confirming tests for the ultimate diagnosis (which are ordered after SAAG determination by current recommendations) may be cost effective to be performed by the results of this point of care test, but this needs to be investigated further in order to determine its cost effectiveness.

Limitations

Our low sample size and fewer patients with a low SAAG ascitic fluid (21 vs 29) were probably the major limitations of this study. Because of these limitations, we preferred not to present a new equation by our data set and use the whole group as a test group for evaluation of the equation introduced by Heidari et al (16). Also, we did not make the researcher blinded to the results of the dipstick test since the results of SAAG were not available immediately. But in the case of therapeutic ascitic taps, the previous diagnosis of patients did not make any bias in the interpretation of the researcher.

Conclusion

Dipstick test of ascitic fluid for pH, glucose, and protein has an acceptable sensitivity and specificity as a point of care test. Further studies with larger populations are needed to recommend for or against its usage as a guide to order further confirmative tests (to identify the cause of cirrhosis) in the ED and decrease the admission time of the patient.

Acknowledgments

This paper was written on the basis of the graduation project of Dr. Leyli Asadabadi, the researcher who participated in designing the study, drafting the manuscript, and gathering the study data. The authors are thankful to Dr. Narges Khanjani for her recommendations on data analysis. Our special thanks are dedicated to Dr. Kamran Heidari, the first author of the inspiring study, who helped us generously and without prejudice to perform the study analysis.

Table 1. Mean (SD) values for glucose, protein, and pH in low SAAG and high SAAG groups

	Laboratory			Dipstick		
	Glucose (mg/dL)	Protein (g/L)	pH	Glucose (mg/dL)	Protein (mg/dL)	pH
Low SAAG	99.8 (74.3)	3.09 (0.8)	7.41 (0.15)	92.3 (52.3)	404.0 (178.3)	7.02 (0.72)
High SAAG	134.5 (66.7)	2.34 (1.7)	7.14 (0.16)	185.4 (68.3)	211.7 (217.1)	7.83 (0.56)
P value	0.09	0.08	<0.0001	<0.001	0.002	<0.001

Abbreviation: SAAG, serum-ascites albumin gradient.

Ethical issues

This study was approved by the Institutional Review Board of Kerman University of Medical Sciences.

Authors' contributions

LA performed data collection, aided in the analysis of the data, and drafted the article. MMH coceived the study, supervised data collection, and aided in drafting of the article. AM conceived the study, performed data analysis, drafted the manuscript, and confirmed the final version of the article.

References

1. Tarn AC, Lapworth R. Biochemical analysis of ascitic (peritoneal) fluid: what should we measure? Ann Clin Biochem 2010; 47(5): 397-407. doi: 10.1258/acb.2010.010048.
2. Mauer K, Manzione NC. Usefulness of serum-ascites albumin difference in separating transudative from exudative ascitic fluid. Dig Dis Sci 1988; 33(10):1208-12. doi:10.1258/acb.2010.010048.
3. Runyon BA, Montano AA, Akriviadis EA, Antillon MR, Irving MA, McHuchinson JG. The serum-ascites albumin gradient is superior to the exudate-transudate concept in the differemtial diagnosis of ascites. Ann Intern Med 1992; 117(3): 215-20. doi: 10.7326/0003-4819-117-3-215.
4. Akriviadis EA, Kapnias D, Hadjigavriel M, Mitsiou A, Goulis J. Serum/ascites albumin gradient: its value as a rational approach to the differential diagnosis of ascites. Scand J Gatroenterol 1996; 31(8): 814-7. doi: 10.3109/00365529609010358.
5. Mansour-Ghanaei F, Shafaghi A, Bagherzadeh AH, Fallah MS. Low gradient ascites: a seven year course review. World J Gastroentrol 2005; 11(15): 2337-9. doi: 10.3748/wjg.v11.i15.2337.
6. Khan J, Pikkarainen P, Karvonen AL, Makela T, Peraaho M, Pehkonen E, et al. Asites: aetiology, mortality, and the prevalence of spontaneous bacterial peritonitis. Scand J Gastroenterol 2009; 44(8): 970-4. doi: 10.1080/00365520902964739.
7. Khandwalla HE, Fasakin Y, El-Searg HB. The utility of evaluating low serum albumin gradient ascites in patients with cirrhosis. Am J Gastroenterol 2009; 104(6): 1401-5. doi: 10.1038/ajg.2009.117.
8. Parsi MA, Atreja A, Zein NN. Spontaneous bacterial peritonitis: recent data onincidence and treatment. Clev Clin J Med 2004; 71(7): 569-76. doi: 10.3949/ccjm.71.7.569.
9. Rerknimitr R, Rungsangmanoon W, Kongkam P, Kullavanijaya P. Efficacy of leukocyte esterase dipstick test as a rapid test in diagnosis of spontaneous bacterial peritonitis. World J Gastroenterol 2006; 12(44): 7183-92.
10. Castellote J, López C, Gornals J, Tremosa G, Fariña ER, Baliellas C, et al. Rapid diagnosis of spontaneous bacterial peritonitis by use of reagent strips. Hepatology 2003; 37(4): 893-9. doi: 10.1016/s0168-8278(02)80151-9.
11. Sapey T, Mena E, Fort E, Laurin C, Kabissa D, Runyon BA, et al. Rapid diagnosis of spontaneous bacterial peritonitis with leukocyte esterase reagent strips in a European and in an American center. J Gastroenterol Hepatol 2005; 20(2): 187-92. doi: 10.1111/j.1440-1746.2004.03554.x.
12. Butani RC, Shaffer RT, Szyjkowsky RD, Weeks BE, Speights LG, Kadakia SC. Rapid diagnosis of infected ascitic fluid using leukocyte esterase dipstick testing. Am J Gastroenterol 2004; 99(3): 532-7. doi: 10.1111/j.1572-0241.2004.04084.x.
13. Bafandeh Y, Khodaei M. Evaluation of leukocyte esterase reagent strip test to detect spontaneous bacterial peritonitis in cirrhotic patients. Gastroentrol Insights 2012; 4(1): e13. doi: 10.4081/gi.2012.e13.
14. Nousbaum JB, Cadranel JF, Nahon P, Khac EN, Moreau R, Thèvenot T, et al. Diagnostic accuracy of the Multistix 8 SG reagent strip in diagnosis of spontaneous bacterial peritonitis. Hepatology 2007; 45(5): 1275-81. doi: 10.1002/hep.21588.
15. Campillo B, Richardet JP, Dupeyron C. Diagnostic value of two reagent strips (Multistix 8 SG and Combur 2 LN) in cirrhotic patients with spontaneous bacterial peritonitis and symptomatic bacterascites. Gastroenterol Clin Biol 2006; 30(3): 446-52. doi: 10.1016/s0399-8320(06)73201-8
16. Heidari K, Amiri M, Kariman H, Bassiri M, Alimohammadi H, Hatamabadi HR. Differentiation of exudate from transudate ascites based on dipstick values of protein, glucose, and pH. Am J Emerg Med 2013; 31(5): 779-82. doi: 10.1016/j.ajem.2013.01.010