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Retrospective Study To Explore A New Predictor For The Early Diagnosis Of Perforated Acute Appendicitis

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Abstract:

Background: Acute appendicitis (AA) is one of the most common indications for emergency abdominal surgery. This case night be complicated by perforation; however, the issue of its diagnosis remains debatable.

Objective: To assess diagnostic and prognostic role of serum bilirubin in the management and diagnosis of perforated acute appendicitis, as well as confirming the relationship between serum bilirubin elevation and appendicitis.

Methods: A data has been collected about Patients diagnosed with acute appendicitis male and females from the age of 4 up to 80 among king Fahad hospital and East Jeddah hospital during the period from 1st Jan 2012 up to 30th July 2017, with sample size of 888 patients.

Results: The study was comprised of 888 consecutive patients. Significance was confirmed as P-value < 0.05. Significance was found upon analyzing direct

bilirubin for all age groups, total bilirubin for age group less than 15 years, direct bilirubin for 15-20 & 21-30 age groups.

Conclusions: Our investigation confirms that bilirubin level might be a biomarker for having appendicitis, it can in some occasions differentiate between types of appendicitis, however, this is not a sharp ending as it has no role in patients within age groups of above 30 years. However, a problem of specificity is present which hinders the adoption of serum bilirubin as a biomarker for perforated AA. In addition, several other methods are more specific for the diagnosis and for choosing the right treatment regimen and the suitable surgery procedure.

KEY WORDS: appendectomy, appendicectomy, appendicitis, bilirubin

Introduction

The analysis of inflamed appendix in its acute condition which is called appendicitis can be tested, and postponed determination may prompt extreme inconveniences, for example, aperture and peritonitis, which are related with high severity. Serum markers, for example, white blood cells count (WBC), C-Reactive Protein (CRP), serum bilirubin, and liver transaminase levels have been proposed as individual markers for an infected appendix and appendiceal aperture (Farooqui et al., 2015, Panagiotopoulou et al., 2013).

In current practice, the analysis of an infected or inflamed appendix in its acute conditions is primarily clinical, upheld by research center and imaging examinations. Computed tomography (CT) and Ultrasonography may raise the indicative affectability or in other words, sensitivity to 66– 100% and 90– 100%, individually, however these practices which are resembled with imaging involve a few disadvantages, for example, cost, radiation presentation, and dependency of the operator (Parks and Schroeppel, 2011).

The delay in AA diagnosis would lead to delay in laparotomy, this delay would cause perforation of the inflamed appendix, and accordingly, increased morbidity (Scher and Coil, 1980, Savrin and Clatworthy, 1979, Harrison et al., 1984).

As of now, no single clinical or research facility test can decide whether a patient has an inflamed ruptured appendix. The surgery rooms do not, generally, manage non-inflamed appendix.

The points of this investigation were to survey the estimation of serum bilirubin in diagnosing perforated AA and anticipating its seriousness.

Literature Review

Appendicitis is a typical introduction with the lifetime danger of appendicitis evaluated at roughly 7% (KW Ma et al., 2010, Weledji, 2016, Shareef et al., 2018, Steele, 2002). At present, a preoperative analysis is a clinical finding dependent on exhaustive history and clinical examination. The clinical evaluation is upheld by biochemical and hematological examinations, for example, WBC and CRP and suitable utilization of radiological examinations, for example, CT checking and stomach ultrasound.

A satisfactory medicinal history joined with clinical examination to inspire basic physical signs related with restricted peritonitis is normally enough to make the determination of acute appendicitis. Be that as it may, the analysis of appendicitis is not the same in every case, particularly, in female patients as a gynecological pathology may impersonate acute appendicitis. Besides, the fluctuation in affixed areas, for example, in retrocecal or hidden appendicitis may not enable patients to show enough peritoneal signs to help the analysis of acute appendicitis (Guidry and Poole, 1994). To date, solid particular marker of acute appendicitis has not yet been distinguished. Notwithstanding progresses in innovation and examination modalities, the rate of negative appendicectomies stays somewhere in the range of 15% and 50% (Khan, 2006).

A few Scoring frameworks have been produced to help in the conclusion of acute appendicitis (Alvaredo (Ohle et al., 2011), Lintula (Lintula et al., 2010) and RIPASA (Chong et al., 2010)). Be that as it may, these frameworks have their own restrictions and are mostly utilized in pediatrics and have not appeared to be exact in the grown-up female population (Ohle et al., 2011).

By and by, the conclusion of acute appendicitis is upheld by the nearness of raised fiery markers, that is, WBC and CRP. Be that as it may, a few examinations have demonstrated that neither of these markers is analytic nor particular for acute appendicitis (Emmanuel et al., 2011).

As of late, serum bilirubin has been found to assume a valuable job in the finding of perforated appendicitis with an affectability of 70% and specificity of 86% (Sand et al., 2009). The symptomatic precision of appendicitis dependent on hyperbilirubinemia stays questionable.

Plainly, an exact conclusion is vital, to anticipate misdiagnosis and superfluous medical procedure as well as to separate straightforward acute appendicitis from a perforated or gangrenous index. Ongoing proof from an expansive multicenter research (Bhangu, 2014) has proposed that patients with appendicitis in its simple form can experience short waiting time in hospital before having their appendicectomy. Nonetheless, the earnest medical procedure is as yet the treatment of decision for confounded (gangrenous/perforated) appendicitis because of the higher rate of comorbidity and confusions and the need to control

the wellspring of sepsis. It is along these lines imperative to stratify patients into those with straightforward appendicitis who can experience medical procedure at a protected chance and those with convoluted appendicitis that require medical procedure all the more desperately.

There has been later restored enthusiasm for the careful writing in regards to the utilization of biomarkers to anticipate clinical determination and various investigations including meta-examination (Al-Abed et al., 2015, Burcharth et al., 2013, Panagiotopoulou et al., 2013, Nomura et al., 2014, Socea et al., 2013, Jamaluddin et al., 2013, Farooqui et al., 2015, Vaziri et al., 2013, Emmanuel et al., 2011, Hong et al., 2012, McGowan et al., 2013, Sand et al., 2009) have recommended that serum bilirubin levels may have a job in recognizing simple acute appendicitis from a perforated or gangrenous reference section. In the event that precise, this would allow the prioritization of patients with perforated appendicitis on working records. It might likewise decrease the quantity of pointless examinations, as patients would advance to the theater.

One of the examinations is supporting the idea of having serum hyperbilirubinemia in the cases of perforated acute appendicitis, while no elevated bilirubin serum level was noticed in simple AA (Khan, 2006). One other study is concluding that serum bilirubin can be considered a positive predictive biomarker, as well as it is sensitive one with regard to perforation in acute appendicitis (Chaudhary et al., 2013).

The aim of this study was to explore a new predictive agent for early diagnosis of perforated appendicitis. This exploration is focused on the level of serum bilirubin and its relationship with the diagnosis of perforated appendicitis.

Materials and Methods

This retrospective study was designed in order to explore a new predictor for the early diagnosis of perforated acute appendicitis.

A data has been collected about Patients diagnosed with acute appendicitis male and females from the age of 4 up to 80 among king Fahad hospital and East Jeddah hospital during the period from 1st Jan 2012 up to 30th July 2017, with sample size of 888 patients.

Data was collected from the records present in the hospital facility and files archives.

Data were analyzed using SPSS software version 22 (SPSS ® Inc, Chicago, USA). Results were expressed in various tables as counts and frequencies. Discrete variables were compared using Chi-square or Fisher exact test as appropriate. A comparison was done for the results of statistical analysis to have a final conclusion of the study. All tests were two-tailed, and a P-value less than 0.05 were deemed to indicate a statistically significant difference.

Results

From a sample size of 888 subjects, results show that 75.6% of the sample are Saudi compared to 24.4% of the sample Non-Saudi, and 69.1% of the sample are males compared to 30.9% females. And when we combine the sample distribution by nationality and by gender, results show that 65.1% of the Saudis in the sample are males while 34.9% of the Saudis in the sample are Females. On the other hand, 81.6% of the Non-Saudis in the sample are Males compared to 18.4% Females.

The average age among the sample is 25.65 years and the median age is 25 years, which means that 50% of the sample is below this age, and 50% of the sample is above this age. In addition, the age in the sample was included within the interval of 4 to 75 years. Within the same area, 37.2% of the sample in the age group from 21 to 30 years old, 22.9% of the sample in the age group from 15 to 20 years old, 18.2 in the age group from 31 to 40 years old, the age group less than 15 years old have only 12.3% and the age group more than 40 years old is 9.3%.

Open surgery operation was adopted for 88.2% of the sample while Laparoscopic operation was done for the rest of the sample (11.8%).

While the diagnosis was one of these three cases: acute appendicitis (51.8%), perforation (37.5%) and abscess formation (10.7%).

The vast majority of the sample was suffering from liver disease with a percentage of 91.7 compared to normal liver disease with a percentage of 8.3.

Direct and total bilirubin were measured and the results show that 63.4% of the patient that the direct bilirubin level observed for them has normal levels of the serum bilirubin (less than 0.3 mg/dl) while 36.6% of those patient suffering from an elevated levels of the serum bilirubin (more than or equal 0.3 mg/dl) while 83.5% of the patient that the total bilirubin level observed for them the serum level from 0.1 to 1.2 mg/dl, compared to 16.5% of those patients the serum level is more than 1.2 mg/dl.

Approximately the elevation compared to normal levels of direct bilirubin was the same when the comparison was done between Saudis and non-Saudis, females and males and different age groups.

Testing all age groups, result of the tests show that the level of bilirubin enzyme (direct bilirubin) is statistically significant with the lab findings of perforated acute appendicitis patients in an ordinal way as the percentage for normal level for the patients suffering from perforated appendicitis was 78.4% while the rest is abnormal in contrast to acute inflammation and abscess formation groups which are having near percentages. As well as a less than 0.05 P-value in Chi-square test.

However, the findings are showing that regarding total bilirubin the results do not differentiate between different appendicitis cases as the percentages of the three types are having an average of 83.2% for the readings ranging from 0.1 to 1.2 mg/dl and the rest are cases with elevated total bilirubin above 1.2 mg/dl. In addition, P-value is above 0.05 upon Chi-square testing which means

statistically insignificant difference between different appendicitis types patients' groups. Nevertheless, after stratifying patients according to age, age group of less than 15 years had shown significant difference regarding total bilirubin when it was compared between different types of appendicitis. Abscess formation was the least percentage of normal range total bilirubin with a percentage of 0.0% and the rest of the sample suffering from abscess formation within this age interval had elevated readings. While perforation had an opposite result with a 100% percentage for normal total bilirubin readings and 0.0% elevated total bilirubin readings.

The findings showed significance for the age group between 15 to 20 as Perforation and abscess formation had most of the patients with normal readings of direct bilirubin (around 80.0%) and the rest were having elevated level. While insignificance was found for total bilirubin.

Significance was found upon the age group of 21 to 30 years when the analysis was done for direct bilirubin levels while total bilirubin had shown insignificance.

And finally, insignificance was the result for the age groups above 30 years old for both direct and total bilirubin levels.

Discussion

Finding of acute appendicitis to a great extent remains a clinical conclusion upheld by research facility and imaging examinations. Albeit a few clinical scoring frameworks have been presented, their exactness stays moderate and like standard clinical judgment (Kollár et al., 2015, Lintula et al., 2010, Mán et al., 2014). The utilization of current imaging may altogether increment symptomatic exactness, yet might be constrained by accessibility, cost, and radiation introduction. Trouble in the finding of acute appendicitis has prompted the persistent look for better indicative markers (Schellekens et al., 2013, Berger et al., 2016) that may diminish radiation introduction and lessen costs.

Our investigation surveyed the analytic viability of bilirubin inside various age bunches in acute appendicitis. Likewise, to the discoveries of D'Souza and associates (D'Souza et al., 2013), our outcomes propose that bilirubin levels may fill in as an imperative indicative factor in specific age groups as well as different results were captured upon comparing total bilirubin and direct bilirubin.

In the course of recent years, a few investigations have proposed serum bilirubin and certain liver catalysts, for example, AST and ALT, as conceivable symptomatic markers for acute appendicitis (Al-Abed et al., 2015, Emmanuel et al., 2011, D'Souza et al., 2013, Panagiotopoulou et al., 2013, Farooqui et al., 2015). A considerably bigger gathering of studies has

concentrated on the relationship of serum bilirubin levels to the seriousness of appendicitis and appendiceal puncturing. An extensive meta-analysis (Giordano et al., 2013) demonstrated high specificity (82%) and a symptomatic chances proportion of 4.42 (95%CI 2.21– 8.83) for raised serum bilirubin levels (more prominent than 1 mg/dl or > 20.5 μmol/l) in diagnosing perforated appendicitis.

Despite the fact that the relationship between raised bilirubin levels and serious appendiceal diseases were portrayed by Miller and Irvine the greater part a century back, the instruments prompting the watched rise in serum bilirubin and liver compounds are yet not completely comprehended. Jaundice and hoisted liver chemical levels have been all around archived in patients with sepsis. The two essential pathogens confined in acute appendicitis are Bacteroides fragilis and Escherichia coli (E. coli) (Bennion et al., 1990), which cause endotoxemia, or, in other words to hepatic dysfunction induced by sepsis. Introduction to E. Coli lipopolysaccharides (LPS) results in a fiery course (Geier et al., 2006), which cause a down-regulation of bile related transporters, diminishes hepatic digestion (McDougal et al., 1978, Ogawa et al., 1982, Sonawane and Yaffe, 1980), and increments nitric oxide synthase (iNOS)- subordinate NO generation, advancing hepatobiliary epithelial boundary brokenness (Han et al., 2004). Moreover, both bacterial species have been appeared to influence with hepatocyte microcirculation, inducing sinusoidal damage in creature models (Rink et al., 1981). The same theory is

supported in (Utili et al., 1977a, Utili et al., 1977b, Utili et al., 1976) regarding the reasons why we are having an elevation in serum bilirubin, and specifically after perforation in inflamed appendix.

It was shown by Sisson et al in 1971 (Sisson et al., 1971) that in a ruptured appendix mucosal ulceration happens early and this encourages intrusion of microscopic organisms into the muscularis propria of the reference section subsequently causing traditional intense suppurative an infected appendix. Resulting occasions prompt edema, raised intraluminal weight, and ischemic putrefaction of mucosa, causing tissue gangrene and puncturing (Bennion et al., 1984b, Bennion et al., 1984a). This procedure is related with dynamic bacterial attack no doubt encouraged by bacterial cytotoxins. The quantity of life forms disconnected from patients with gangrenous or perforated appendix is five times more prominent than those with intense suppurative an infected appendix. Estrada et al (Estrada et al., 2007) likewise found fundamentally higher peritoneal culture in patients with gangrenous/perforated an infected appendix.

A few top notches think about were distributed pushing nonoperative administration for acute appendicitis in particular settings (Di Saverio et al., 2014). In the Non-Operative Treatment for Acute Appendicitis (NOTA) examine (Varadhan et al., 2012), the fleeting achievement rate of anti-infection treatment in speculated appendicitis was 88% with no major adversities recorded for patients with starting treatment disappointments. Nonetheless,

translation of these outcomes needs to think about conceivable predisposition from the patient populace with relative lack of serious introductions (mean AIR score = 4.9, mean Alvarado score = 5.2).

Conclusion

Our investigation confirms that bilirubin level might be a biomarker for having appendicitis, it can in some occasions differentiate between types of appendicitis, however, this is not a sharp ending as it has no role in patients within age groups of above 30 years. However, a problem of specificity is present which hinders the adoption of serum bilirubin as a biomarker foe AA. In addition, several other methods are more specific for the diagnosis and for choosing the right treatment regimen and the suitable surgery procedure.

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