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RESEARCH ARTICLE

COMPARATIVE STUDY OF DISEASE SEVERITY, COURSE, COMPLICATIONS, AND CLINICAL OUTCOME BETWEEN ALCOHOL-INDUCED PANCREATITIS AND GALL STONE-INDUCED PANCREATITIS

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Abstract

Objective: To assess whether the etiological factors of alcohol and gall stones affect the disease severity, course, disease-associated complications, and clinical outcome in terms of length of hospital stay, infection/organ failure rates, intervention rates, and mortality.

Materials and Method: We conducted a hospital-based prospective study in the Department of Radio-Diagnosis, Assam Medical College, where 75 cases with acute pancreatitis were screened and subdivided into three etiological groups: (i) alcoholism (33 cases), (ii) cholelithiasis (23 cases), and (iii) other causes (19 cases), out of which 56 cases with etiology of alcoholism and gall stones were included in our study. The severity was scored using the Modified CT Severity Index. Clinical follow-up was done for both alcohol-induced Pancreatitis and Gall stone-induced pancreatitis groups to assess the disease course, disease-associated complications& clinical outcome.

Statistical analysis: We analyzed data using the computer program Statistical Package for Social Sciences (SPSS for Windows, version 21.0. Chicago, SPSS Inc.) and Microsoft Excel 2010.

Results: In a total of 75 cases screened for our study, alcohol-induced pancreatitis was the leading cause of acute pancreatitis (33 cases), followed by gall stone-induced pancreatitis (23 cases). Together, they accounted for 56 cases and constituted our study population. The majority of cases in our study were categorized under Moderate acute Pancreatitis in both alcohol-induced acute pancreatitis and gall stone-induced Pancreatitis as per the Modified CT Severity Index. The occurrence of ascites was more in alcohol-induced A.P. No significant difference was noted between the two groups in parameters such as peripancreatic or pancreatic fluid collection, necrosis, pleural effusion, extrapancreatic parenchymal abnormality, vascular complications & G.I. complications. There was no statistically significant difference in clinical outcome between the two groups regarding the length of hospital stay, infection/organ failure evidence, need for intervention, and mortality.

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Conclusion: Our study found no significant difference between the two etiological groups regarding disease severity, course & complications, and clinical outcome except for the increased occurrence of ascites in alcohol-induced pancreatitis.

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Introduction:-

The annual incidence of acute pancreatitis ranges from 13 to 45 per 100 000 people[1]. Acute pancreatitis is a condition causing acute inflammation of the pancreas and frequently involves the peripancreatic tissues and sometimes remote organ systems with a variable clinical outcome. Disease manifestation of acute pancreatitis varies from mild forms that only affect the pancreas to severe forms causing multisystemic organ failure and death. The major pathobiological processes that underlie acute pancreatitis are inflammation, edema, necrosis of pancreatic tissue, and inflammation and injury of the extrapancreatic organs [2]. The two leading causes for acute Pancreatitis are Gallstone-related pancreatitis and Alcohol related-pancreatitis. Together cholelithiasis and alcoholism account for 76% of pancreatitis cases [3]. Although the basic pathophysiology of pancreatitis, irrespective of the etiology, is premature activation of the digestive enzymes within the acinar cell, causing autodigestion, the triggering event for the two etiologies vary[4].

Gallstone-related Pancreatitis is the most common cause and is estimated to be 28%-38% of all cases of acute pancreatitis[5]. It is caused by duct obstruction by gallstone migration leading to impaction of migrated stones at the level of duodenal ampulla, increased duct pressure, and unregulated stimulation of the digestive enzymes secreted by the pancreas[6]. This obstruction can be due to fibrosis of the sphincter of Oddi[7]

Alcohol related-pancreatitis is the second most frequent cause and is estimated to be 19%-41% of all acute pancreatitis[8]. Alcohol causes reduced blood flow and free radical damage within the pancreas[4]. 2/3rd cases who present with acute alcohol related-pancreatitis already have developed an underlying chronic pancreatitis[9]. In about 8% of alcohol-induced-pancreatitis cases, mutations in the pancreatic secretory trypsin inhibitor gene (SPINK1) have also been seen[10]. In our study, alcohol-induced pancreatitis was the leading cause of pancreatitis.

About 15%-20% of cases with Acute Pancreatitis will develop severe disease and will have an elongated hospital stay with complications including possible death[11]. Thus, determining the severity of A.P. is one of the most important first steps in managing A.P. since it helps select appropriate treatments, ensure proper patient triage, initiate appropriate therapies, and stratify patient risk for complications [12].

In this study, we have tried to assess whether the specific etiology of alcoholism or gall stones will have an independent effect on the disease severity, course, disease-related complications, and clinical outcome to stratify cases accordingly and give timely management. The severity scoring was done with the help of the Modified CT Severity Score.

Materials And Methods:-

This study was a Hospital-based prospective study conducted over one year in the Department of Radio-Diagnosis, Assam Medical College and Hospital. We screened seventy-five cases referred from various clinical departments with suspected acute pancreatitis based on increased serum lipase and amylase activity. We subdivided them into three etiological groups(i) alcohol-induced pancreatitis group (33 cases), (ii) gall stone-induced pancreatitis group (23 cases), and (iii) other causes (19 cases), out of which 56 cases with etiology of alcohol and gall stones were included in our study. We excluded cases with other causes or overlapping etiologies of acute pancreatitis from the study & cases with a history of pre-existing chronic pancreatitis. Also, we excluded cases with deranged renal functions, pregnant cases & cases with a known history of allergy to iodinated contrast agents. The demographic, radiographic, and laboratory data of these cases were collected prospectively as per institute protocol, and the data were analyzed.

The institute's ethics committee approved the study, and we obtained written informed consent from all cases.

Case Definition For Diagnosis Of Acute Pancreatitis[13]

For diagnosis of acute pancreatitis, two of the following three features were required:

1. Abdominal pain that is consistent with acute pancreatitis (acute onset of a persistent, severe, epigastric pain often radiating to the back).
2. Serum lipase activity (or amylase activity) that is at least three times greater than the upper limit of normal.
3. Findings that are characteristic of acute Pancreatitis on CECT imaging.

We categorized cases as alcohol-induced pancreatitis when there was a history of alcohol consumption of approximately 50–80 g/day of alcohol, irrespective of gender, for five years or more or alcoholic binge drinking one week before the onset of the disease with a lack of evidence of other causes.

We categorized cases as gall stone-induced pancreatitis when imaging findings were suggestive of Gall stone or biliary sludge on ultrasonography, C.T., or endoscopic ultrasound.

Severity assessment

We did CECT Abdomen in cases who met the inclusion criteria, and the Modified CT Severity index helped in severity assessment.

Modified CT Severity index

Prognostic Indicator	Points
Normal pancreas	0
Intrinsic pancreatic abnormalities with or without inflammatory changes in peripancreatic fat	2
Pancreatic or peripancreatic fluid collection or peripancreatic fat necrosis	4
Pancreatic Necrosis	
None	0
<30%	2
>30%	4
Extrapancreatic complications (one or more of pleural effusion, ascites, vascular complications or gastrointestinal tract involvement)	2

1. 0 – 2: mild acute Pancreatitis
2. 4 – 6: moderate acute Pancreatitis
3. 8- 10: severe acute pancreatitis.

Patient Follow-Up:

We followed up with the cases to assess the clinical course and outcome.

Outcome Measures:

The various outcome measures included length of hospital stay, evidence of infection/organ failure, need for intervention, and mortality

Statistical Analysis:

We analyzed data using the computer program Statistical Package for Social Sciences (SPSS for Windows, version 21.0. Chicago, SPSS Inc.) and Microsoft Excel 2010. Continuous measurements were presented as mean and standard deviation and were compared using the student t-test. Discrete data were expressed as numbers (%) and were analyzed using the Chi-square test and Fischer's exact test (where the cell counts were <5 or 0). We fixed the statistical significance at a 5% level (p-value <0.05).

Results:-

We included 56 cases in our study, in which 33 cases constituted alcohol-induced pancreatitis group, and 23 cases constituted gall stone-induced pancreatitis group.

Demographic Parameters:

Table 1:- Comparison Between Pancreatitis Induced By Alcohol And Gall Stone According To Age And Gender.

VARIABLE	ALCOHOL (n = 33) n (%)	GALL STONE (n = 23) n (%)
Age (Mean ± S.D.) (in years)	38.58 ± 12.68	38.87 ± 12.68
Gender:		
1. Male	31 (93.94%)	11 (47.83%)
2. Female	2 (6.06%)	12 (52.17%)

The mean age of cases with alcohol-induced Pancreatitis & Gall stone-induced pancreatitis was 38.58 ± 12.68 & 38.87 ± 12.68, respectively. There was male predilection in the alcohol-induced pancreatitis group accounting for 93.94% of cases, and female predilection in the Gall stone-induced pancreatitis group accounting for 52.17% of cases.

Table 2:- Comparison Between Pancreatitis Induced By Alcohol And Gall Stone According To Modified Ct Severity Index.

MCTSI		ALCOHOL (n = 33) n (%)	CHOLELITHIASIS (n = 23) n (%)	p value
Mild	0–2	3 (9.09%)	4 (17.39%)	0.3555
Moderate	4–6	20 (60.61%)	16 (69.56%)	0.4912
Severe	8–10	10 (30.30%)	3 (13.04%)	0.1323
Mean ± S.D.		5.94 ± 2.52	4.96 ± 2.25	0.1321

The majority of cases in our study were categorized under Moderate acute Pancreatitis in both alcohol-induced acute pancreatitis and gall stone Pancreatitis. In alcohol-induced A.P., the incidence of severe acute pancreatitis was comparatively higher (30.30 % vs. 13.04%, P = 0.1323) but was not statistically significant. Therefore, the severity of disease was similar between the two groups using the Modified CT Severity index.

Disease Course And Complications

Table 3:- Comparison Between Pancreatitis Induced By Alcohol And Gall Stone According To The Following Parameters.

VARIABLE	ALCOHOL (n = 33) n (%)	CHOLELITHIASIS (n = 23) n (%)	p value
Peripancreatic or Pancreatic Fluid Collection	25 (75.76%)	16 (69.57%)	0.6067
Necrosis	10 (30.30%)	3 (13.04%)	0.1323
Ascites	18 (54.55%)	6 (26.09%)	0.0343
Pleural Effusion	12 (36.36%)	11 (47.83%)	0.3910
Vascular Complications	3 (9.09%)	2 (8.70%)	0.9394
GI Complications	3 (9.09%)	1 (4.35%)	0.4977

1. Occurrence of ascites was more in alcohol-induced A.P (54.55% vs. 26.09%, P = 0.0343).
2. No significant difference was noted between the two groups in parameters such as peripancreatic or pancreatic fluid collection, necrosis, pleural effusion, vascular complications & G.I. complications.
3. In alcohol-induced A.P., a comparatively higher necrosis rate was noted (30.30 % vs. 13.04%, P = 0.1323) but was not statistically significant.

Clinical Outcome

Table4:- Comparison Between Pancreatitis Induced By Alcohol And Gall Stone According To The Following Parameters:

VARIABLE	ALCOHOL (n = 33) n (%)	CHOLELITHIASIS (n = 23) n (%)	p value
Hospital Stay (Mean ± S.D.)(in days)	12.09 ± 7.38	9.96 ± 6.16	0.2455
Infection	2 (6.06%)	1 (4.35%)	0.7795
Organ Failure	6 (18.18%)	1 (4.35%)	0.1236
Intervention	9 (27.27%)	2 (8.70%)	0.0852
Death	1 (3.03%)	0	0.2898

We compared outcome parameters such as length of hospital stay, infection/organ failure evidence, need for intervention, and mortality between the two groups. There was no statistically significant difference between the two groups.

However, in the alcohol-induced pancreatitis group, the rate of intervention was slightly higher when compared to the Gall stone-induced pancreatitis group but not statistically significant.

Discussion:-

We conducted this study in the department of Radiodiagnosis, Assam Medical College, and Hospital over 12 months. We screened 75 cases with acute pancreatitis based on increased serum lipase and amylase activity prospectively. We subdivided them into three etiological groups (i) alcohol-induced pancreatitis group (33 cases), (ii) gall stone-induced pancreatitis group (23 cases), and (iii) other causes (19 cases), out of which 56 cases with etiology of alcohol and gall stones were included in our study. We compared the severity of Acute Pancreatitis in the two etiology groups using the Modified CT Severity Index, followed up the cases, and assessed clinical outcome parameters (Length of hospital stay, evidence of infection/organ failure, need for intervention, and mortality) to compare the two groups.

Demographic Parameters:

Age:

The mean age of cases with alcohol-induced Pancreatitis &Cholelithiasis-related Pancreatitis was 38.58 ± 12.68 & 38.87 ± 12.68, respectively, similar to the study conducted by **JayantaSamanta et al.**[14], in which the mean age of cases with alcohol-induced Pancreatitis &Cholelithiasis-related Pancreatitis was 37.08 ± 9.9 and 43.29 ± 14.8 respectively. Also, our study correlates with the study conducted by **Shivanand S. Melkundi et al.**[15], where most of the cases belonged to the 31-40 age group.

Etiology:

In our study, alcohol was the leading cause of acute pancreatitis, similar to the study conducted by**Shivanand S. Melkundiet al.** [15]and**JayantaSamantaet al.**[14]**,** in which alcohol was the leading cause of acute pancreatitis. Also, together cholelithiasis and alcoholism accounted for 74.6 % of all cases that were screened in our study, similar to the study conducted by **Irshad Ahmad Bandayet al.**[3], where they found cholelithiasis and alcoholism to account for 76% of cases.

Gender predilection:

Female predilection was noted in Gall stone-induced pancreatitis (52.17%) and male predilection in alcohol-induced pancreatitis (93.94%), similar to a study conducted by **JayantaSamantaet al.**[14]**&Atsushi Masamuneet al.** [16] in which they found that alcoholic A.P. was most common in males and gallstone A.P. was the most common in female cases.

Severity Assessment:

The majority of cases in our study were categorized under Moderate acute Pancreatitis in both alcohol-induced acute pancreatitis and gall stone Pancreatitis using the Modified CT Severity Index. In alcohol-induced A.P., the incidence of severe acute pancreatitis was comparatively higher (30.30 % vs. 13.04%, P = 0.1323) but was not statistically significant. Therefore, the severity of disease was similar between the two groups using the Modified CT Severity index.

We did not find relevant literature where the Modified CT Severity Index was used to compare disease severity assessment between the two groups, probably due to very few studies done after the Modified CT Severity index development. Modified CT Severity index predicts clinical outcomes better than that obtained with CT Severity index while maintaining or improving the interobserver agreement[17]. Thus in our study, we used Modified CT Severity Index for assessing the severity of acute pancreatitis.

JayantaSamantaet al.[14]used APACHE-II,Systemic Inflammatory Response Syndrome (SIRS), and Bedside Index for Severity in A.P. (BISAP), and The CT severity index (CTSI) for disease severity assessment. They found the two groups' severity parameters, such as SIRS, BISAP, APACHE II at admission, CTSI, and the Atlanta classification, to be similar. **Joon Hyun Cho et al**.[18] compared disease severity between the two groups using APACHE-II, BISAP, Ranson score, and CT severity index (CTSI). CTSI showed a statistically significant difference in scoring systems between the two groups. No significant differences in Ranson, BISAP, and APACHE-II scores were observed between the alcohol group and the gall stone group

Disease Course

Various studies have pointed out higher development rates of local complications like peripancreatic fluid collection &pseudocyst formation among the alcohol-induced pancreatitis group. **Dae BumKim et al**.[19]found higher rates of peripancreatic fluid collection, and **Joon Hyun Cho et al**.[18]highlighted more significant pseudocyst formation in the alcohol group. However, in our study, there was no statistical difference between the two etiological groups regarding the development of pancreatic or peripancreatic fluid collections/pseudocysts (75.76% vs. 69.57 %, P = 6.067).

In our study, alcohol-induced A.P. had higher necrosis rates when compared to the cases with Gall stone-induced A.P. (30.30 % vs. 13.04%, P = 0.1323). However, it was not statistically significant. Development of necrosis is higher in the alcohol-induced pancreatitis group, as per studies done by **JayantaSamantaet al.** [14]. In another study by **W Uhl et al.**[20], necrosis rates are similar in both the etiological groups.

Our study found a significant difference in ascites between the two groups, with more incidence in the alcoholic group. However, in the study conducted by **JayantaSamantaet al.** [14], there was no significant statistical difference between the two groups.

In our study, there was no significant difference in the occurrence of other complications likepleural effusion, extrapancreatic parenchymal complications, vascular complications, and gastrointestinal complications between the two groups. We did not find relevant pieces of literature that compared these complications between the two groups.

Clinical Outcome

1. Length of Hospital stay: In our study, there was no statistical difference between the two groups regarding the length of hospital stay, similar to studies done by **Joon Hyun Cho et al.** [18] and **JayantaSamantaet al.** [14].
2. Infection/organ failure: In our study, there was no statistical differencebetween the two groups in terms of infection/ Organ failure, similar to study done by **JayantaSamantaet al.**[14] and **W Uhl et al.**[20]
3. Intervention: In our study, in the alcohol-induced pancreatitis group, the rate of intervention was slightly higher when compared to the Gall stone-induced pancreatitis group but was not statistically significant (27.2% vs. 8.7%, p=0.0852). As per the study done by **JayantaSamantaet al.**[14], there was no statistical difference in surgical intervention between the two groups. However, the need for percutaneous catheter drainage was more in the case of alcohol-induced pancreatitis.
4. Mortality: In our study, there was no statistical difference between the two groups in terms of mortality similar to the study done by **W Uhl et al.**[20], **Andersen A et al.** [21], and **JayantaSamantaet al.**[14].

Conclusion:-

Whether specific etiology contributes to the disease course, disease-related complications, or clinical outcome in patients with Acute Pancreatitis is an unresolved issue. In this regard, various studies have reported different results based on the two main etiological groups causing acute pancreatitis: alcohol and gallstone. Our study found no significant difference between the two groups regarding disease course and complications except for the increased occurrence of ascites in alcohol-induced pancreatitis. Also, the clinical outcome regarding the length of hospital stay, infection/organ failure evidence, need for intervention, and mortality of acute pancreatitis was independent of

the etiology. Therefore, we imply that once the disease's pathobiological mechanisms start, no matter the triggering event, the course and outcome of acute pancreatitis are not influenced by the underlying etiological factor.

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