RESEARCH ARTICLE

A COMPARISON OF OUTCOMES BETWEEN UNCOMPLICATED AND COMPLICATED APPENDICITIS. CAN A RATIONAL APPROACH OF INJECTABLE ANTIBIOTICS BE APPLIED FOR UNCOMPLICATED APPENDICITIS? - A SINGLE CENTRE EXPERIENCE.

Basu Shouptik¹, Kirtania Dona¹ and Jana Debarshi².
1. Basu Shouptik - MBBS (Hons), MS (General Surgery), Department of General Surgery, Bankura Sammilani Medical College and Hospital.
2. Kirtania Dona – MBBS , MD (Anaesthesiology), Department of Anaesthesiology, Bankura Sammilani Medical College and Hospital.
3. Jana Debarshi-PhD, Young Scientist, Young Scientist (DST), Department of Gynecology and Obstetrics, Institute of Post-Graduate Medical Education and Research, A.J.C. Bose Road, Kolkata-700020, West Bengal, India.

Manuscript Info

Abstract

Background: Acute appendicitis is the most common surgical emergency in young adults. A delayed presentation of a patient with uncomplicated appendicitis may progress to a complicated appendicitis (appendicular phlegmon, gangrene, perforation abscess, localized or generalized peritonitis). Emergency Surgery is the standard of care.

Material and Methods: We have prospectively analysed 167 patients with proper informed consent to participate in the study, having satisfied our inclusion criteria. 86 patients had uncomplicated appendicitis and 81 had complicated appendicitis. The presentation and surgical outcomes of both these clinical entities were compared and the feasibility of a rational dose of single day course of antibiotics has been evaluated statistically.

Results and Analysis: Of 167 patients the majority of patients were within the age group of 11-20, 65(38.9%), with a slight female predominance. Of the 81 patients with complicated appendicitis 45.7% presented with a Phlegmon. Mean days of symptoms of patients in complicated appendicitis, was 3.1852 ± 0.8531 days compared to 1.5698 ± 0.4980 days uncomplicated. Most of the complicated cases had fever during presentation. Mean operative time (40.6914 ± 10.3388 mins), incidence of wound infection (22%), ileus (29.6%) is more in complicated appendicitis. There was one case of Faecal fistula. The mean duration of antibiotics is more in complicated appendicitis 9.1975 ± 3.4728 days versus 3.5116 ± 2.9773 days leading to prolonged stay (5.7160 ± 2.7894 days) in complicated cases. Complicated appendicitis patients have more morbidity (Clavien-Dindo score >1). 50 patients out of 85 patients (58%) with uncomplicated appendicitis were given a rationally justified, single day dose of antibiotics, without any complications. Hence the prognoses of such patients were better leading to minimal morbidity.
Conclusion: Complicated Appendicitis must be managed surgically with a prolonged course of Antibiotics, where as a single day regime of rationally justified course of antibiotics can be successfully instilled in patients with uncomplicated appendicitis to decrease the burden due to morbidity.

Introduction:-
Acute Appendicitis is the frequent cause of an Acute Abdomen that requires surgical management, leading to hospital admissions. Although once considered vestigial the immunological role of the appendix cannot be completely denied. Earlier Appendicectomy was considered as a standard of care, due to the fear of a perforated appendix [1] An Uncomplicated appendicitis would be an inflamed appendix that is grossly intact, non-gangrenous without any suppuration or signs of peritonitis. The definition of Complicated Appendicitis has not been described well in literature but it would refer to an appendicular phlegmon, gangrene, abscess localized or generalized peritonitis. [2-5]. Now there has been a paradigm shift towards a conservative (Non-operative) approach for Acute appendicitis. [6] In many centres traditional open surgery has been abandoned and Laparoscopic Surgery [7] is becoming the standard of care. However, the role of a Classical Open Mc.Burney’s approach [8] to the appendix cannot be denied.

The Infectious Diseases Society of America recommends against postoperative antibiotic therapy beyond 24 hours for uncomplicated intra-abdominal infection. [9] However, prolonged antibiotic administration is common despite intra-operative diagnosis of uncomplicated appendicitis. There are no definite guidelines in India regarding the duration of antibiotics for acute appendicitis. Experiences vary in between institutions. Most of our patients present late and the number of Emergency surgeries for complicated appendicitis are on the rise in our institution.

We undertook this descriptive study to identify pre- and intra-operative factors predicting prolonged antibiotic administration in appendicitis. We have summarized the presentation of our patients from the data that we have collected over the last year in a single unit from a teaching Medical Institution in West Bengal, India. We aim to compare the outcomes of Acute appendicitis from our institute and have also tried to evaluate whether our patients would benefit from a Rational single day course of Antibiotics for uncomplicated Appendicitis

Materials And Methods:-
Our institution is a high volume tertiary referral teaching hospital. Ethical Clearance to conduct the study was obtained from the Intuitional Ethics committee. The work has been carried out according to the Code of Ethics in the Declaration of Helsinki for experiments involving human subjects. We and have prospectively analysed patients that have presented in our Emergency department and have been diagnosed with Acute Appendicitis from June 2017 to May 2018.

Inclusion criteria: Patients diagnosed with acute appendicitis belonging to ASA Grade I to III who can be taken up for surgery were included in the study, after a proper informed consent and their signature.

Exclusion criteria: Patients with severe systemic disease, those unwilling to participate in the study, and those belonging to ASA Grade IV and later and well defined appendicular lumps were excluded from the study.

Demographics, presenting symptoms like fever, duration of surgery and intra operative findings were evaluated and documented. The correlation of intra operative findings of complicated appendicitis such as phlegmon, gangrene, perforation abscess, Localized and Generalized peritonitis have been recorded and compared. Patients with complicated appendicitis have been administered Injectable Antibiotics like Ceftriaxone Igim Intravenous Infusion along with Metronidazole Infusion as per their dosage recommendations. The duration of administration depended upon the requirement and clinical response of patients. Post-operative parameters such as Ileus, Fever, Beginning of oral intake and wound infection have been evaluated. The morbidity of the patient on Injectable Antibiotics was analysed using thClavien-Dindo [10] scoring system where a value of > 1 would be considered significant. The relation of the use of antibiotics to the duration of hospital stay has been analysed. Finally, our aim to evaluate the outcomes for a rational use of Antibiotics use for Uncomplicated Appendicitis has been tabulated using Microsoft Excel and statistically analysed using SPSS 24.0.
Statistical Analysis:-
For statistical analysis data were entered into a Microsoft excel spreadsheet and then analyzed by SPSS 24.0. and GraphPad Prism version 5. Data had been summarized as mean and standard deviation for numerical variables and count and percentages for categorical variables. Two-sample t-tests for a difference in mean involved independent samples or unpaired samples. Paired t-tests were a form of blocking and had greater power than unpaired tests. A chi-squared test ($\chi^2$ test) was any statistical hypothesis test wherein the sampling distribution of the test statistic is a chi-squared distribution when the null hypothesis is true. Without other qualification, 'chi-squared test' often is used as short for Pearson's chi-squared test. Unpaired proportions were compared by Chi-square test or Fischer’s exact test, as appropriate. $p$-value ≤ 0.05 was considered for statistically significant.

Result And Analysis:-
In our study 18(10.8%) patients were ≤10 years, 47(28.1%) patients were within the age group of 11-20, 65(38.9%) patients were in between 21-30 years of age, 33(19.8%) patients were within 31-40 years of age and 4(2.4%) patients were in the age group of 41-50. The majority of our patients being female 94 (56.3%) to 73(43.7%) males. 81(48.5%) patients suffered from Complicated Appendicitis and 86(51.5%) patients had Uncomplicated. Amongst the complicated group 37(45.7%) patients had Phlegmon, 24(30.0%) patients had Localized Peritonitis 3(3.7%) patients had Generalized Peritonitis, 13(16.0%) patients had Gangrenous Appendicitis, 3(3.7%) patients had Abscess, and 9(11.1%) patients had Perforation.

Mean days of symptoms such as anorexia, nausea or vomiting pain in the Right lower quadrant of the abdomen (mean± s.d.) of patients in complicated appendicitis, was 3.1852 ±.8531 days with a range OF 2.00-6.00 days and the median was 3.00 days. In uncomplicated appendicitis, the mean days of symptoms (mean± s.d.) of patients were 1.5698 ±.4980 days with range 1.0000 -2.0000 days and the median was 2.0000 days. Difference of mean age in two groups was statistically significant (p<0.0001). Almost all our complicated appendicitis patients 81(100.0%) had fever during presentation, compared to the 26(30.2%) patients belonging to the uncomplicated group. This association was statistically significant (p<0.0001). Presentation with fever alleviates the necessary use of antibiotics and thus the post-operative morbidity increases.

In complicated appendicitis, mean operative time (mean± s.d.) of patients was 40.6914 ±10.3388 mins with a range 20.0000 -70.0000 mins and the median was 40.0000 mins. In uncomplicated group, The mean operative time of symptoms (mean± s.d.) of patients was 24.8140 ±4.6615 mins with range 18.0000-47.0000 mins and the median was 25.0000 mins. Difference of mean age in two groups was statistically significant (p<0.0001).

Wound Infection is a fairly common occurrence in patients with complicated appendicitis was 18 (22.2%) compared to 1(1.2%) patient who had wound infection in uncomplicated group. This association was statistically significant (p=0.000019). One patient developed a faecal fistula 1 (1.2%). This result wasn’t statistically significant. 24(29.6%) patients with complicated appendicitis had Ileus compared to 5(5.8%) in uncomplicated group, which was considered statistically significant (p=0.000005). 39(48.1%) of complicated appendicitis patients had post-operative fever compared to 36(41.9%) patients with uncomplicated appendicitis. This association was not statistically significant (p=0.6665).

In complicated appendicitis patients required an increase in, duration of antibiotics (mean± s.d.) of patients was 9.1975 ±3.4728 days with range 5.0000 -28.0000 days and the median was 7.0000 days. In uncomplicated appendicitis, duration of antibiotics of symptoms (mean± s.d.) of patients was 3.5116 ±2.9794 days with range 1.0000 -7.0000 days and the median was 1.0000 days. Difference of mean age in two groups was statistically significant (p<0.0001).

Complicated appendicitis patients could tolerate the beginning of oral intake (mean± s.d.) by 32.8889 ±14.9131 hours with range 24.0000 -96.0000 hours and the median was 24.0000 hours. Compared to the patients with uncomplicated appendicitis, which was 24.5581 ±3.6384 hours with range 24.0000 -48.0000 hours and the median was 24.0000 hours. Difference of mean age in two groups was statistically significant (p<0.0001).

In complicated appendicitis, length of stay (mean± s.d.) of patients was 5.7160 ±2.7894 days with range 3.0000 -28.0000 days and the median was 5.0000 days. In uncomplicated appendicitis, length of stay of symptoms (mean± s.d.) of patients was 3.0465 ±3.032 days with range 3.0000-5.0000 days and the median was 3.0000 days. Difference of mean age in two groups was statistically significant (p<0.0001).
In uncomplicated appendicitis receiving antibiotics post-surgery had their morbidity evaluated by the Clavien-Dindo Scoring system. Here, 51(59.3%) patients had score 1, 34(39.5%) patients had score 2 and 1(1.2%) patient had score 3. Complicated Appendicitis patients however, had 63(77.8%) patients with score 2 and 18(22.2%) patients had score 3. This association was statistically significant (p<0.0001).

50 patients out of 85 patients (58%) with uncomplicated appendicitis were given a rationally justified, dosage of antibiotics. Hence the prognosis of such patients were better leading to less morbidity. The rest 36 had post-operative complications that augmented the duration of antibiotics (average 7 days).

Discussion:-
Acute appendicitis, the most common pathology requiring Emergency surgery is perhaps the first case a surgical resident is taught to perform independently. Appendicitis, is the most common cause of acute abdomen in a young adult. presents classically with Murphy’s triad, namely periumbilical pain, with associated nausea, vomiting and anorexia. There may be associated fever. The pain gradually shifts to the Right Iliac Fossa as the uncomplicated appendicitis tends to become complicated with more inflammation. It progresses to an appendicular phlegmon with localized peritonitis. If the Greater omentum is unable to seal the infection, as in children, old age, immunocompromised adults to form an appendicular lump the appendix perforated and may cause generalized or localized peritonitis or a pelvic abscess. Various scoring system have been developed in the past that correlate severity of the disease. The ALVARDO score is perhaps the most commonly used parameter before surgery. Radiological tests such as an Ultrasound and Contrast Enhanced CT scan are ancillary investigations when the score is equivocal (5-6) a score of >7 is considered as Appendicitis and surgery may be planned.[11]. In our study the patients have been categorised as Complicated and Uncomplicated based upon their initial presentation [12] and duration of symptoms. Many centres prefer a conservative approach to Acute appendicitis but our institution considers Open Emergency Surgery as the standard of care.

Most of our patients present late and the mean duration of symptoms of progression from an uncomplicated to an appendicular lump is approximately 4 days. Complicated appendicitis patients deteriorate clinically and present with more symptoms that need to be detected on clinical examination. A decision for surgery must be prompt. Appendicular lumps if not certain are to be evaluated under anaesthesia. Complicated Appendicetomies require more time, there is no difference in surgical outcomes between Senior consultants and Residents when it comes to time. Meticulous hemostasis is essential an a drain may be left in the pelvis if a possible collection or an appendicular abscess is detected. Wound infection is common after surgery specially due to the contact of the infected phlegmatogenous contents with the wound site. Faecal fistulas are rare but they occur. [8,11]

Ileus is fairly common after surgery (30% as in our case) and are given oral feeds once the bowel sounds resume. Our study shows an increase in ileus amongst complicated cases because of the tendency of the inflamed appendix to form a lump with the adjoining loops of bowel. Post-operative fever is a sign of infection and requires rigorous use of antibiotics. Most patients are discharged by 5-6 days and are requested to return after 7-10 days for stich removal.

There is no doubt that complicated antibiotics require a better antibiotic support. However, uncomplicated appendicitis can be controlled with a minimum rational dose of Antibiotics to prevent patient morbidity. Out of all 86 patients suffering from uncomplicated appendicitis, 50 patients (58%) were given a rationally justified, dosage of antibiotics. Hence the prognosis of such patients was better leading to less morbidity.

Conclusion:-
Delayed presentation with complicated appendicitis requires a more rigorous surgical approach and a course of antibiotics, leading to a longer post-operative recovery. When patients present early with uncomplicated appendicitis a rational approach of minimum duration of antibiotics may be tried after surgery since a prolonged course of antibiotics may augment the morbidity of the patient.

Acknowledgements:-
The authors would like to acknowledge the Department of General Surgery and Department of Anaesthesiology, BankuraSammillani Medical College and Hospital for their help and support. The authors would also like to thank the Residents and Consultant surgeons of Unit III Surgery, Emergency OT staff nurses for their help for the article, and the patients who have participated in the study for their help.
Table 1: Demographics and distribution of Causes for Complicated Appendicitis

| Age (Range) | Frequency | Percentage |
|-------------|-----------|------------|
| ≤10         | 18        | 10.8%      |
| 11-20       | 47        | 28.1%      |
| 21-30       | 65        | 38.9%      |
| 31-40       | 33        | 19.8%      |
| 41-50       | 4         | 2.4%       |

| Sex         |            |            |
|-------------|-----------|------------|
| Female      | 94        | 56.3%      |
| Male        | 73        | 43.7%      |

| Complicated (C) or Uncomplicated (UC) | Frequency | Percentage |
|--------------------------------------|-----------|------------|
| Uncomplicated                        | 86        | 51.5%      |
| Complicated                          | 81        | 48.5%      |

Figure 1: Distribution of Cases with Complicated Appendicitis

Distribution of cases with Complicated Appendicitis

Table 2: Distribution of parameters with Uncomplicated and Complicated Appendicitis

|                          | Complicated | Uncomplicated | TOTAL | Chi-square value | p-value |
|--------------------------|-------------|---------------|-------|------------------|---------|
| Fever during Presentation|             |               |       |                  |         |
| NO                       | 0           | 60            | 60    | 88.2004          | <0.0001 |
| Row %                    | 0.0         | 100.0         | 100.0 |                  |         |
| Col %                    | 0.0         | 69.8          | 35.9  |                  |         |
| YES                      | 81          | 26            | 107   |                  |         |
| Row %                    | 75.7        | 24.3          | 100.0 |                  |         |
| Col %                    | 100.0       | 30.2          | 64.1  |                  |         |
| TOTAL                    | 81          | 86            | 167   |                  |         |
| Row %                    | 48.5        | 51.5          | 100.0 |                  |         |
| Col %                    | 100.0       | 100.0         | 100.0 |                  |         |
| Wound Infection          |             |               |       |                  |         |
| NO                       | 63          | 85            | 148   | 18.3475          | 0.000019|
| Row %                    | 42.6        | 57.4          | 100.0 |                  |         |
| Col %                    | 77.8        | 98.8          | 88.6  |                  |         |
| YES                      | 18          | 1             | 19    |                  |         |
| Row %                    | 94.7        | 5.3           | 100.0 |                  |         |
| Col %                    | 22.2        | 1.2           | 11.4  |                  |         |
| TOTAL                    | 81          | 86            | 167   |                  |         |
| Row %                    | 48.5        | 51.5          | 100.0 |                  |         |
| Col %                    | 100.0       | 100.0         | 100.0 |                  |         |
| Faecal Fistula           |             |               |       |                  |         |
| NO                       | 80          | 86            | 166   | 1.0681           | 0.3013  |
| Row %                    | 48.2        | 51.8          | 100.0 |                  |         |
Table 3: Mean Distribution of parameters with Uncomplicated and Complicated Appendicitis

|                          | C      | UC     | Mean  | SD   | Minimum | Maximum | Median | p-value |
|--------------------------|--------|--------|-------|------|---------|---------|--------|---------|
| **Days of Symptoms**     | 81     | 86     | 3.1852| .8531| 2.0000  | 6.0000  | 3.0000 | <0.0001 |
| **Operative Time (Mins)**| C      | 81     | 40.6914| .4980| 18.0000 | 70.0000 | 25.0000| <0.0001 |
| **Duration of Antibiotics (days)** | C      | 81     | 9.1975| .34728| 24.0000 | 28.0000 | 7.0000 | <0.0001 |
| **Beginning of Oral Intake (Hours)** | C      | 81     | 32.8889| 4.9131| 24.0000 | 96.0000 | 24.0000| <0.0001 |
| **Length of Stay (Days)** | C      | 81     | 5.7160| .3032| 3.0000  | 5.0000  | 3.0000 | <0.0001 |

Figure 2: Association of Morbidity (Clavien-Dindo Score) with Use of Antibiotics in Uncomplicated Appendicitis
[Clavien-Dindo score 1 is considered as Good prognosis and >1 is Poor prognosis]
Figure 3: Uncomplicated Appendicitis
Figure 4: Gangrene of the tip in a Complicated Appendicitis

Figure 5: Appendicular Perforation
Conflicts Of Interest: The authors declare that they have no conflicts of interest.

Funding: None

References:
1. Brunicardi F Charles, Andersen Dana K, Billiar Timothy R, Dunn David L, Hunter John G. Schwartz’s Principles of Surgery. Tenth edition. New York: McGraw-Hill Education, The Appendix. pp.1241-62.
2. Rahman GA, Debrah SA. Complicated appendicitis: experience from central region of Ghana. IntSurg J 2018;5:277-80.
3. Operative versus non-operative management in the care of patients with complicated appendicitis Helling, Thomas S. et al. The American Journal of Surgery. Volume 214, Issue 6, 1195 - 1200
4. Kong VY, Bulajic B, Allorto NL, Clarke DL. Acute Appendicitis in a Developing Country World. J Surg. 2012;36:2068-73
5. Pittman-Waller VA, Myers JG, Stewart RM, Dent DL, Page CP, Gray GA, et al. Appendicitis: Why so complicated? Analysis of 5755 consecutive appendectomies. Am Surg. 2000;66:548.
6. Findlay, John M. et al. Nonoperative Management of Appendicitis in Adults: A Systematic Review and Meta-Analysis of Randomized Controlled Trials Journal of the American College of Surgeons. Volume 223, Issue 6, 814- 824.e2
7. Arias, F. (n.d.). Management of Complicated Appendicitis: Is Laparo-endoscopic Single Site Surgery (less) a Safe Option? - SAGES Abstract Archives.
8. Fischer JE. Fischer’s Mastery of Surgery: Appendicitis and Appendiceal Abscess. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2012. p. 1603-06.
9. Joseph S. Solomkin, John E. Mazuski, et al; Diagnosis and Management of Complicated Intra-abdominal Infection in Adults and Children: Guidelines by the Surgical Infection Society and the Infectious Diseases Society of America, Clinical Infectious Diseases, Volume 50, Issue 2, 15 January 2010, Pages 133–164.
10. Dindo D, Demartines N, Clavien P. Classification of Surgical Complications: A New Proposal With Evaluation in a Cohort of 6336 Patients and Results of a Survey. Ann Surg. 2004 Aug; 240(2): 205–213.

11. Russell RC, Norman WS, Bulstrode JK. Bailey and Love’s Short Practice of Surgery: The Vermiform Appendix. 26th ed. London: CRC Press; 2013. p. 1199-1214.

12. Serres, Stephanie K. et al. Influence of Time to Appendectomy and Operative Duration on Hospital Cost in Children with Uncomplicated Appendicitis. Journal of the American College of Surgeons, Volume 226, Issue 6, 1014 – 1021.