



INCIDENCE AND PREDICTORS OF NEGATIVE APPENDECTOMY: A RETROSPECTIVE OBSERVATIONAL STUDY

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ABSTRACT

Background: Negative appendectomy, defined as the removal of a histologically normal appendix, remains a measurable source of avoidable morbidity. It is difficult to identify patients with a very low probability of true appendicitis before committing them to surgery. The aim of this study was to determine the institutional incidence of negative appendectomy and identify clinical, biochemical, as well as imaging and scoring parameters able to discriminate these patients.

Methods: This was a retrospective observational study done in Indira Medical College and Hospitals, covering a three-year period from October 2022 to October 2025 for all patients undergoing appendectomies. Two hundred and twenty patients were found to meet the eligibility criteria for the study. Histopathological examination of resected specimen constituted the diagnostic gold standard, while clinical scoring (Alvarado and Appendicitis Inflammatory Response [AIR] scores) was calculated. Independent samples t-test, Fisher's exact test and Mann-Whitney U analysis were employed for statistical inference. A p-value of <0.05 was considered statistically significant in a two-tailed test.

Results: Of the cases, five (2.27%; 95% CI: 0.30%–4.24%) found on final histopathology to have a histologically normal appendix constituted the negative appendectomy group. Compared to confirmed appendicitis, patients undergoing negative appendectomy had significantly lower leucocyte counts ($8,587.2 \pm 1,289.8$ vs $14,926.6 \pm 2,344.0$ cells/ μ L; $p < 0.001$), a lower percentage of neutrophils ($59.0 \pm 4.2\%$ vs $83.1 \pm 5.2\%$; $p < 0.001$), and lower C-reactive protein (10.4 ± 3.4 vs 54.5 ± 19.9 mg/L; $p < 0.001$). Alvarado scores for all negative cases ranged 5 to 6, while they ranged 8.4 ± 1.1 in the positive group ($p < 0.001$). AIR scores ranged from 3 to 5 in all negative cases and was higher in positive patients at 10.2 ± 1.4 , ($p < 0.001$). Ultrasonography was positive for appendicitis in all confirmed cases, but positive in negatives ($p < 0.001$). No statistical significance was picked for simply age and sex.

Conclusion: A negative appendectomy rate of 2.27% augurs well for the institute. Lower clinical scores (Alvarado ≤ 6 , AIR ≤ 5), only modest leucocytosis with mild neutrophilia, near normal CRP and absence of sonographic evidence of appendicitis are the most robust measurable predictors of unnecessary appendectomy. The addition of mandatory scoring threshold with cross-sectional imaging for equivocal cases is believed to hold significant value to eliminating the residual negative appendectomy rate.

Keywords: Negative Appendectomy, Appendicitis Inflammatory Response Score, Alvarado Score, C-reactive Protein, Leucocytosis, Ultrasonography.

INTRODUCTION

Acute appendicitis is the commonest cause of an emergency laparotomy at all ages, with a lifetime incidence in the population estimated as between seven and eight per cent.[1]

Appendectomy-either open or laparoscopic-remains the definitive management of clinically diagnosed appendicitis.[2] Despite many years of further investigation prior to surgery, a number of patients undergoing appendectomy are found at histological examination of that organ to have had a macroscopically and microscopically normal appendix. This phenomenon, termed in the literature a negative appendectomy, represents a complication resulting from failure to adequately predict diagnosis pre-operatively, leading to patients suffering the hazards of general anaesthesia and



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surgical procedure, and possible post-operative complications, without therapeutic gain.[3]

Negative appendectomy rates have varied by year and unit, and before the widespread use of cross-sectional imaging tended to be in the range of fifteen to twenty five per cent in the literature.[4] Negatives were significantly reduced with introduction of helical CT to three to eight per cent in recent series dependent upon the protocol, socio-demographics of the patients and experience of the surgeons.[4-6] The waste of unnecessary appendectomies has an economic impact; Flum and Koepsell showed using nationwide data that false positive 'tools' such as appendicitis trigger excessive costs for hospitalisation, and independently are associated with increased post-operative complications.[4] Some authors have argued against a zero negative appendectomy rate as the counterbalancing measure for perforation rate. If we aim for a zero negative appendectomy rate then diagnosed perforating cases of appendicitis may be unduly delayed in overly conservative surgery.[7] The true delicately judged reference point therefore lies somewhere between avoiding unnecessary surgery and preventing delayed diagnosis.

Two scoring systems are widely used in current practice for risk stratification of suspected acute appendicitis. The Alvarado score was first published in 1986 and covers eight clinical and laboratory findings-migration of pain to right iliac fossa, anorexia, nausea or vomiting, tenderness in right iliac fossa, rebound tenderness, higher temperature, leucocytosis, and left shift of differential count-to give a maximum score of ten.[8] A score of 7 or above is assumed to give high probability of appendicitis and sufficient for patient warranting operative intervention and likewise a score of four or below would indicate low probability and guide the clinician to observation or discharge.[8] The Appendicitis Inflammatory Response (AIR) score was suggested by Andersson and Andersson in 2008 as an amendment, adding CRP (another inflammatory marker) and using a weighted scoring structure demonstrating better stratification of disease severity than Alvarado system in several validation studies.[9,10] Both systems have been validated prospectively in multicentre cohorts and are recommended in current consensus guidelines.[11] Ultrasonography is commonly the first line imaging modality for evaluation of suspected appendicitis especially in children and women in particular due to the absence of ionising radiation.[12] Its sensitivity for appendicitis is variable and operator-dependent ranging from seventy-five to ninety percent in published meta analysis.[13] CT scanning will do better (>95%) plus specificity, but is associated with concerns regarding radiation exposure particularly in the younger population. Further it is not universally the first investigation in all centres and resource

settings.[5] MRI has emerged as an alternative imaging modality with high levels of accuracy with no elemental radiation dose to the patient. Unfortunately availability and cost prohibit it from routine use currently.[14] Predictors of negative appendectomy described in the literature include female sex owing to potential overlap with gynaecological diagnoses, also, younger age, atypical presentation of pain, lower leucocyte counts, lower CRP levels, negative or equivocal imaging studies, and lower clinical scores.[3,6,15] The relative weights of different predictors and appropriate cutpoints for intervention differ between populations and institutions and knowledge of local incidence and correlate predictors is essential to institute local quality improvement protocols.

We designed this study to: Determine the incidence of negative appendectomy in a cohort of consecutive appendectomies operated at a tertiary care surgical centre over a thirty six month period. Compare clinical, biochemical, imaging and scoring parameters that differ statistically between confirmed appendicitis and negative appendectomy. Assess the discriminative capacity of the Alvarado and AIR scores in our population.

MATERIALS AND METHODS

Design and setting

We conducted a retrospective observational study, at the Department of General Surgery, Indira Medical College and Hospitals (IMCH), Puducherry, a tertiary care teaching institution between October 2022 and October 2025 (36 months). Anonymous subject data were retrieved, with prior approval from the Institutional Ethics Committee. Since this was a retrospective study and archival patient records were de-identified, a waiver of informed consent was obtained. It follows the principles of the Declaration of Helsinki.

Eligibility Criteria

Inclusion criteria: All patients (irrespective of age and sex) who underwent appendectomy, for suspicion of acute appendicitis (clinically) during the study period; where records contained clinical notes, laboratory reports, imaging "findings", notes from the procedure and the histopathological results.

Exclusion Criteria

Patients who underwent incidental appendectomy during any of the several primary surgical procedures; patients who underwent interval appendectomy, following convergence period of conservative (antibiotic) treatment for presumed appendicitis; patients wherein the appendectomy was for non-inflammatory use (which means that it was due to malignancy, or mucocele); in cases where there was no available histopathology (incomplete/missing).

Data Collection

Retrospective data access was through the medical records, files of cases attending to the emergency department, the operation theatre register, report of radiology, report of laboratory information system, and histopathology archives; demographic data (age, sex), clinical data (migration of pain, anorexia, nausea or vomiting, fever, tenderness in right iliac fossa, rebound tenderness), laboratory indices (WBC/TLC, Neutrophil %, CRP), USG findings (reported as Appendix present (Yes/No), procedure notes, and histopathology diagnosis, etc. Based on the clinical and laboratory data recorded in the file, we calculated Alvarado and AIR scores.

Outcome Definitions

Negative appendectomy: Histopathological examination showing a normal appendix, without any evidence of acute inflammation (neutrophilic infiltration in wall), suppuration, gangrene, perforation, or other appendicular pathology.

Positive (Confirmed) Appendicitis

Histopathological examination confirming the diagnosis of appendicitis, being Acute (Catarrhal) Appendicitis, Suppurative Appendicitis, Gangrenous Appendicitis or Perforated Appendicitis, i.e. inflammatory changes Joint to an Appendicolith (Appendicolith).

Sample Size

The study population is all Consecutive Cases of appendectomies done during the year (n = total 220). Our pre-study sample size estimation, based on the estimated prevalence of Negative Appendectomies of 15.5% (derived from Noureldin et al) [15] of the year 2022, with a confidence level of 95%, and a precision of 5% then requires a minimum of 196 patients. We aimed to study 10% over and above this number or suitably; as it turned out our enrolment is in excess of this number.

Statistical analysis: Analyses were performed using IBM SPSS Statistics (version 26.0; IBM Corp, Armonk, NY). The main outcome the negative appendectomy rate was expressed as a proportion and the 95% confidence interval (CI) was calculated by normal approximation (Wald). Continuous variables were expressed as mean ± standard deviation. Differences in means between groups were assessed using the independent samples t-test. Categorical variables were expressed as frequencies with percentages and for those with expected count < 5, Fisher's exact test was used. The discriminative capability of the continuous predictors was measured as area under receiver operating characteristic (ROC) curve (AUC) via Mann-Whitney U statistic. A two-tailed p-value < 0.05 was considered statistically significant.

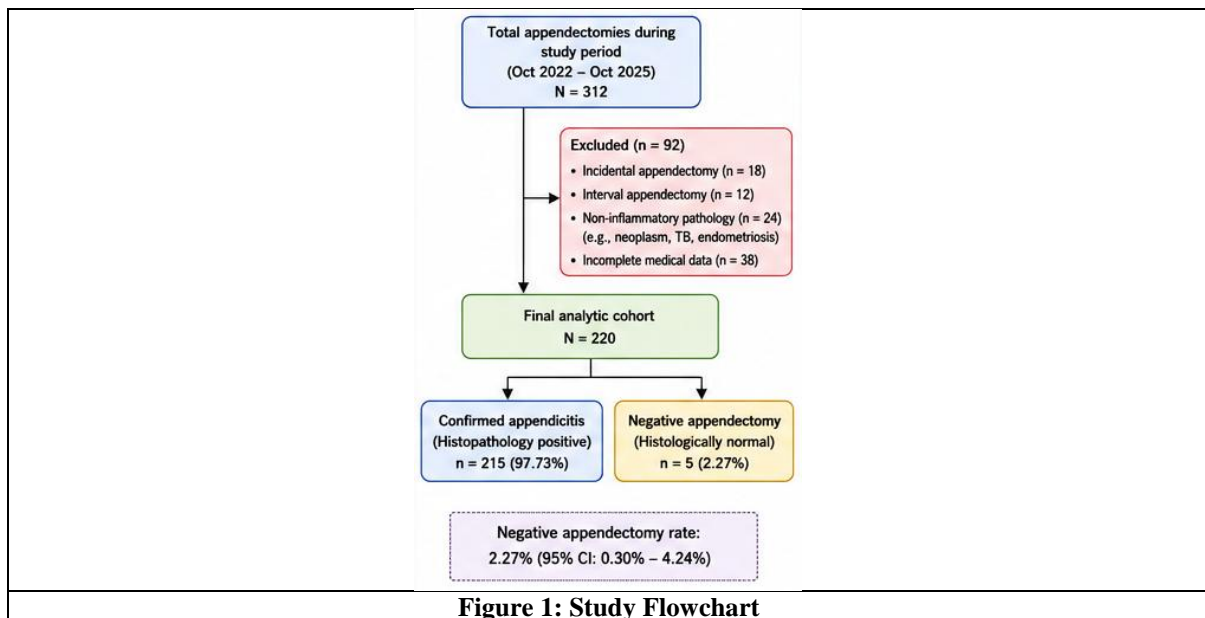


Figure 1: Study Flowchart

RESULTS

Two hundred and twenty patients satisfied the eligibility criteria and were included in the analysis. Histopathological examination confirmed appendicitis in 215 cases (97.7%). Five patients

(2.27%; 95% CI: 0.30%–4.24%) had a histologically normal appendix and constituted the negative appendectomy group. Baseline demographic characteristics are presented in **Table 1**.

Variable	Total (n = 220)	Confirmed Appendicitis (n = 215)	Negative Appendectomy (n = 5)
Age (years), Mean ± SD	34.9 ± 12.1	35.0 ± 12.2	31.8 ± 6.1
Age group			
≤ 20 years	35 (15.9%)	35 (16.3%)	0 (0.0%)
21–40 years	99 (45.0%)	94 (43.7%)	5 (100%)
> 40 years	86 (39.1%)	86 (40.0%)	0 (0.0%)
Sex			
Female	119 (54.1%)	116 (54.0%)	3 (60.0%)
Male	101 (45.9%)	99 (46.0%)	2 (40.0%)

Table 1. Baseline Demographic Characteristics of the Study Cohort
SD: standard deviation

Among the 215 confirmed appendicitis cases, gangrenous appendicitis was the most prevalent histological diagnosis (n = 69; 32.1%), followed by acute catarrhal appendicitis (n = 56; 26.0%),

perforated appendicitis (n = 46; 21.4%), and suppurative appendicitis (n = 44; 20.5%). The complete histopathological distribution is shown in **Table 2**.

Histopathological Diagnosis	n	Percentage (%)
Gangrenous appendicitis	69	32.1
Acute (catarrhal) appendicitis	56	26.0
Perforated appendicitis	46	21.4
Suppurative appendicitis	44	20.5
Normal appendix (negative appendectomy)	5	2.3
Total	220	100.0

Table 2. Histopathological Distribution of Appendectomy Specimens (n = 220)

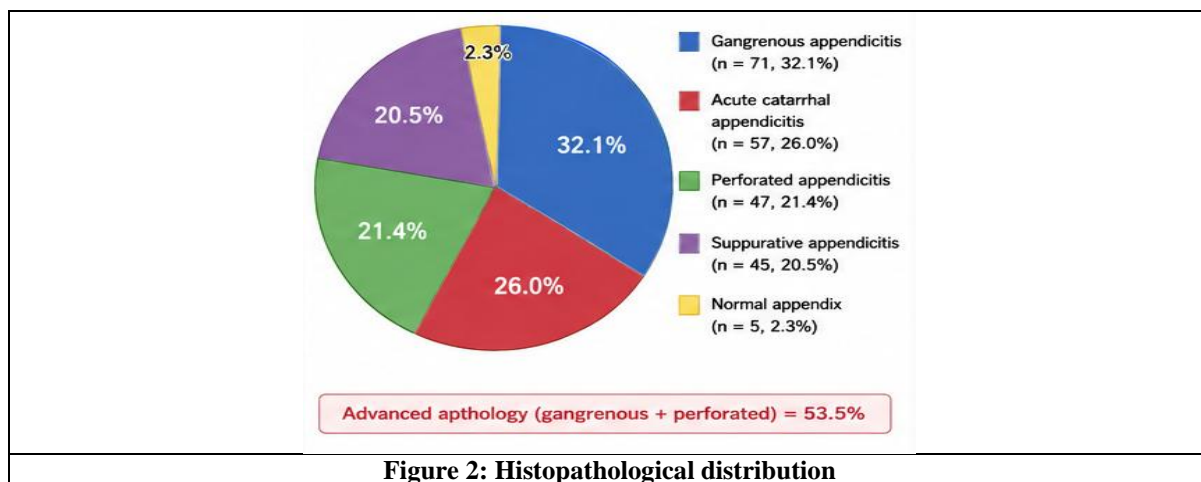


Figure 2: Histopathological distribution

All key biochemical parameters and clinical scores were significantly elevated in confirmed appendicitis compared with negative appendectomy cases (Table 3). The mean total WBC was 14,926.6 ± 2,344.0 cells/μL in the positive group versus 8,587.2 ± 1,289.8 cells/μL in the negative group (p < 0.001). Mean neutrophil percentage was 83.1 ± 5.2% versus 59.0 ± 4.2% (p < 0.001), and mean CRP was 54.5 ± 19.9 mg/L versus 10.4 ± 3.4 mg/L (p < 0.001). Each of these variables achieved a perfect area under the ROC curve (AUC = 1.000) in discriminating between groups, reflecting complete separation of the value ranges between confirmed and negative cases.

The mean Alvarado score in the positive group was 8.4 ± 1.1 (range 7–10) compared with 5.4 ± 0.5

(range 5–6) in the negative group (p < 0.001). The mean AIR score was 10.2 ± 1.4 (range 8–12) in confirmed appendicitis versus 4.0 ± 0.7 (range 3–5) in negative cases (p < 0.001). All five negative appendectomy patients had an Alvarado score ≤6 and an AIR score ≤5—ranges that correspond to the equivocal or low-probability categories in both scoring systems. Ultrasonography was reported as positive for appendicitis in all 215 confirmed cases (100%) but in only 2 of the 5 negative cases (40%), a statistically highly significant difference by Fisher's exact test (p < 0.001). Age was not significantly different between groups (35.0 ± 12.2 vs 31.8 ± 6.1 years; p = 0.564), nor was the sex distribution (p = 1.000).

Parameter	Confirmed Appendicitis (n=215) Mean ± SD	Negative Appendectomy (n=5) Mean ± SD	p-value	AUC
WBC (cells/μL)	14,926.6 ± 2,344.0	8,587.2 ± 1,289.8	< 0.001	1.000
Neutrophil percentage (%)	83.1 ± 5.2	59.0 ± 4.2	< 0.001	1.000
CRP (mg/L)	54.5 ± 19.9	10.4 ± 3.4	< 0.001	1.000
Alvarado Score	8.4 ± 1.1	5.4 ± 0.5	< 0.001	1.000
AIR Score	10.2 ± 1.4	4.0 ± 0.7	< 0.001	1.000
Age (years)	35.0 ± 12.2	31.8 ± 6.1	0.564	—
USG positive, n (%)	215 (100%)	2 (40%)	< 0.001 †	—

Table 3. Comparison of Clinical and Biochemical Parameters Between Groups

† Fisher's exact test applied. AUC: area under the receiver operating characteristic curve; CRP: C-reactive protein; USG: ultrasonography; WBC: total leucocyte count.

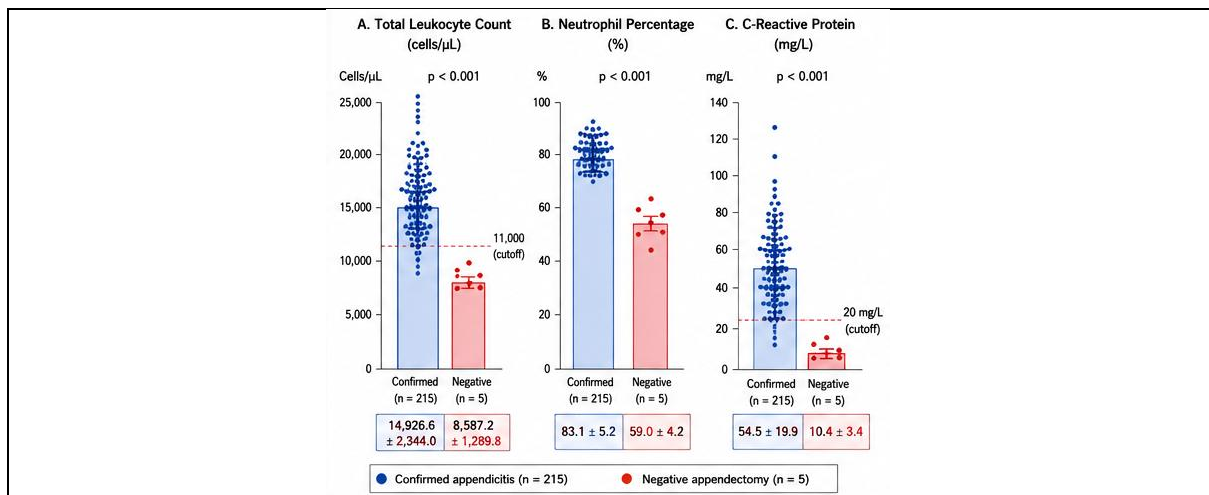


Figure 3: Comparison of Biochemical parameters between groups

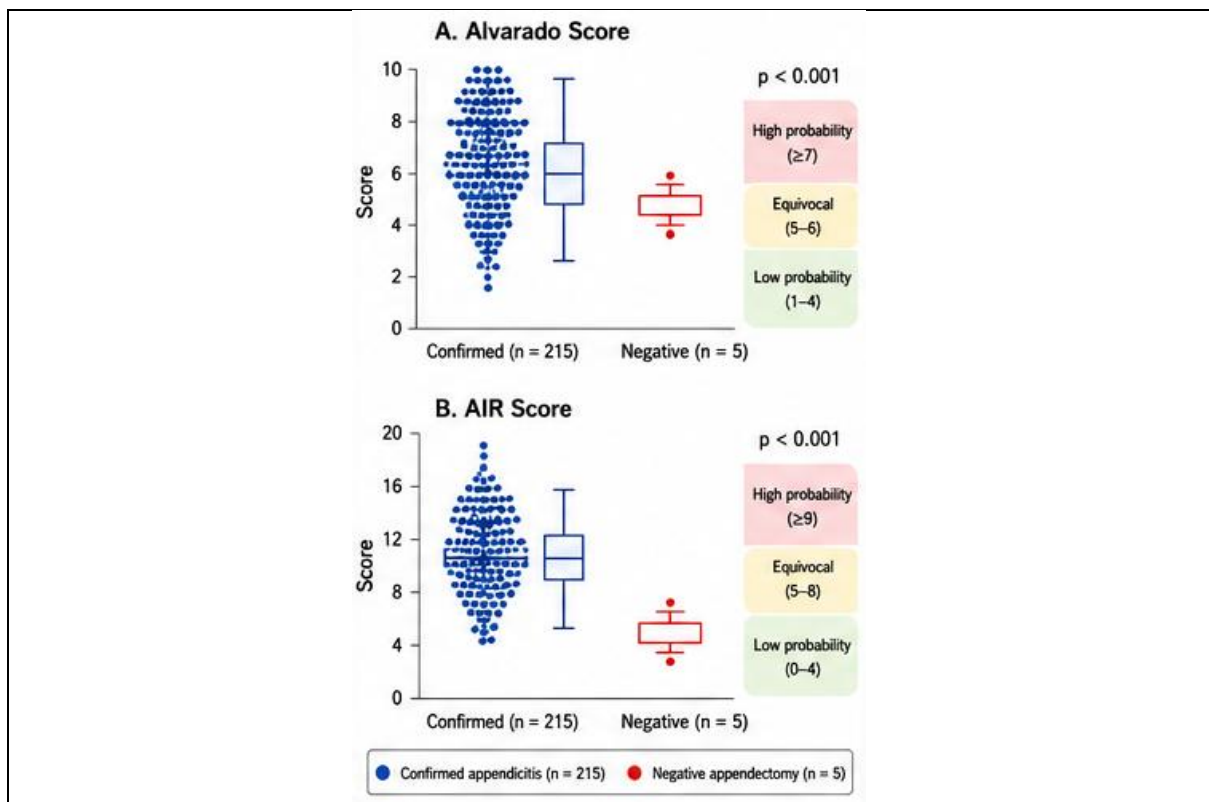


Figure 4: Clinical score distribution

The demographic and laboratory profiles of the five negative appendectomy patients are detailed in **Table 4**. Their ages ranged from 23 to 38 years (three female, two male). Total WBC ranged from 7,018 to 10,163 cells/ μ L, neutrophil percentage from 55% to 66%, and CRP from 7 to 15 mg/L-

values substantially below those recorded in confirmed appendicitis cases. Three of the five had a negative ultrasonogram yet proceeded to surgery on the basis of clinical assessment. All five cases returned a histopathological report of normal appendix without inflammatory change.

Case	Age	Sex	WBC (μ L)	Neutrophil (%)	CRP (mg/L)	Alvarado Score	AIR Score	USG
1	31	F	7,018	58	9	6	4	Negative
2	38	M	9,284	59	15	5	4	Negative
3	30	M	8,934	55	13	5	3	Positive
4	37	F	7,537	57	8	6	5	Positive
5	23	F	10,163	66	7	5	4	Negative

Table 4. Individual Profiles of Negative Appendectomy Cases
USG: ultrasonography finding (positive or negative for appendicitis)

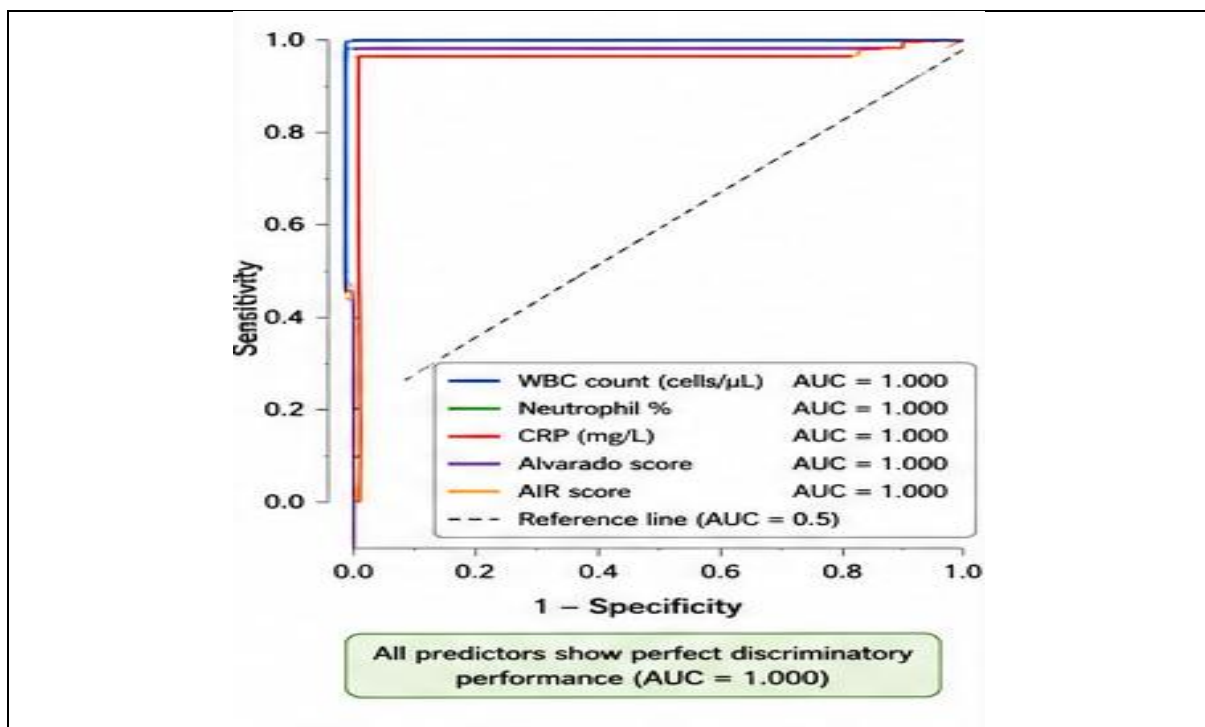


Figure 5: ROC curves for key predictors

DISCUSSION

The present study describes a negative appendectomy rate of 2.27% (95% CI: 0.30–4.24%) over 36 months of 220 consecutive appendectomies, which is comparable to both historical and contemporary published series. Prior to the introduction of readily available abdominal CT, negative appendectomy rates of fifteen to twenty five per cent have been described from North American and European centres.^[4] Flum and Koepsell have noted that misdiagnosis of appendicitis - that is, both including negative appendectomies as well as perforation - is associated with longer hospital stay and increased complications - the need for evidence based diagnosis in both directions.^[4] Once CT came into routine use, rates fell sharply in centres that had

ready access. De Dombal showed, using decision-support tools, that even clinical collection of structured data could significantly impact negative appendectomy rates, long before the use of imaging.^[16]

In a roughly contemporaneous series from the UK, Noureldin et al found a rate of 15.5% with female sex and younger patients more likely to undergo unnecessary surgery.^[15] Livingston et al showed in a very large data set from North America that CT scanning lowered negative appendectomy rates from 17% with physical exam alone to 8%, at the same time lowering perforation rates.^[5] Bhatt et al described a rate of 9.7% in a paediatric cohort emphasising the diagnostic challenge of children.^[6] The lower rate of the present series, at 2.27%, is lower than all the comparisons made, and is one

reflection of our combined use of clinical scoring combined with ultrasound in our institutional diagnosis scheme. Bhangu et al., in their definitive review of the pathogenesis and management of acute appendicitis in *The Lancet*, found that the ideal negative appendectomy rate lies between one and five per cent; low enough to assure that high-probability cases are not being delayed, but not so high as to imply over-diagnosis. Our institution's rate falls comfortably in that stream.

The clinical scoring data in this series are of particular note. All five negative appendectomy patients had Alvarado scores of five or six, the equivocal (indeterminate) range of four to six whereby the original validation study advised further observation and investigation rather than definitive operative intervention. Likewise, all five had AIR scores of three to five, again in the low-probability or indeterminate stratum of the AIR classification scale, whereby they would have been best either discharged home for outpatient follow-up or followed up with repeat assessment by the authors' recommendations. The mean AIR score of 10.2 ± 1.4 in confirmed appendicitis cases and 4.0 ± 0.7 in negative cases represent more than six points separation across group comparisons, far exceeding that needed for perfect discriminative performance (AUC = 1.000) in this cohort-the result warrants some caution since the number of negative cases was small. Scott et al. proved in a prospective multicentre validation study that the AIR: score "exhibits superior discriminative ability" to the Alvarado score, in stratifying appendicitis into simple or complicated and distinguishing those amenable A CRP of less than 20 mg/L was seen in all five negative appendectomy cases versus a mean CRP in confirmed appendicitis of 54.5 mg/L. This is consistent with the pathophysiology of appendiceal inflammation whereby bacterial translocation and mucosal ischaemia causes hepatic acute-phase response with CRP rise in the first twelve to twenty-four hours from onset of symptoms.^[17] In early or mild appendicitis this can only be slight, but CRP consistently sub upper limit of normal laboratory should raise diagnostic suspicion before surgical commitment. Andersson et al. showed in a systematic review that CRP over twenty-five mg/L increases Likelihood ratio for appendicitis considerably but less than this figure contributes to its exclusion.^[18] Neutrophil % in negative cases (mean 59.0%) were less than the minimum that could be found in any confirmed case, further emphasising its utility for discrimination when combined with scoring data.

The importance of ultrasonography as gatekeeper to surgery in this cohort is apparent. Three of the five negative appendectomy cases had a negative report on ultrasonography but all three had operation. There are situations where clinical judgement

should rightly override investigation in certain presentations - a limited sonographic window due to body habitus or bowel gas, or lack of operator experience fall into this category - but these cases caution against the risk of embarking upon an operation on marginal clinical probability without sonographic or CT correlation. Published meta-analyses show ultrasound sensitivity for appendicitis in the range of 75–90%, with specificity of 86–94%, with significant operator dependence.^[13] A negative ultrasound in the setting of a low AIR or Alvarado score should prompt CT or a period of structured observation with repeated clinical staging, as per a number of national guidelines and WSES consensus document.^[11] García Peña et al. showed that a structured pathway combining a clinical score followed by selective CT if indeterminate can reduce the negative appendectomy rate to below three per cent in a prospective cohort.^[19] The histopathological distribution of patients with confirmed appendicitis in this series reveals that advanced disease was noted in a substantial number: gangrenous appendicitis was found in 32.1% of cases and perforated appendicitis in 21.4%, for a combined rate of advanced pathology of 53.5%. This is grossly higher than the rates of 20–30% seen in many Western series, reflecting the nature of the demographic served by the institution, which saw a number of patients present after longer periods. This bears on the debutante factors which lend itself to a low negative appendectomy rate; a high proportion of advanced pathology presents because institutional case-mix means that clearer clinical diagnoses likely favour the path of least resistance through the preoperative diagnosis. Conversely, it reinforces the importance of rapid surgical intervention once the diagnosis is made, since delay in this group carries a considerable risk of perforation and peritonitis.^[2] Female sex has been described as a negative appendectomy risk factor in several large series, principally because ovarian and tubo-ovarian pathology can closely simulate acute appendicitis, both clinically and sonographically.^[3,15] In our cohort, three out of five (60%) negative appendectomies were female; a mild relative over-representation due to the 54.1% female representation in the full cohort, but unlikely to be significant at this magnitude. Baird et al described an almost doubled rate of negative appendectomy in women between the ages of fifteen and forty-five, and recommended mandatory gynaecology assessment or at least pelvic ultrasound scan prior to appendectomy in that population.^[3] The future introduction of a structured gynaecological triage of women of childbearing age who present with right iliac fossa pain might further assist in minimising schedule of appendectomy.

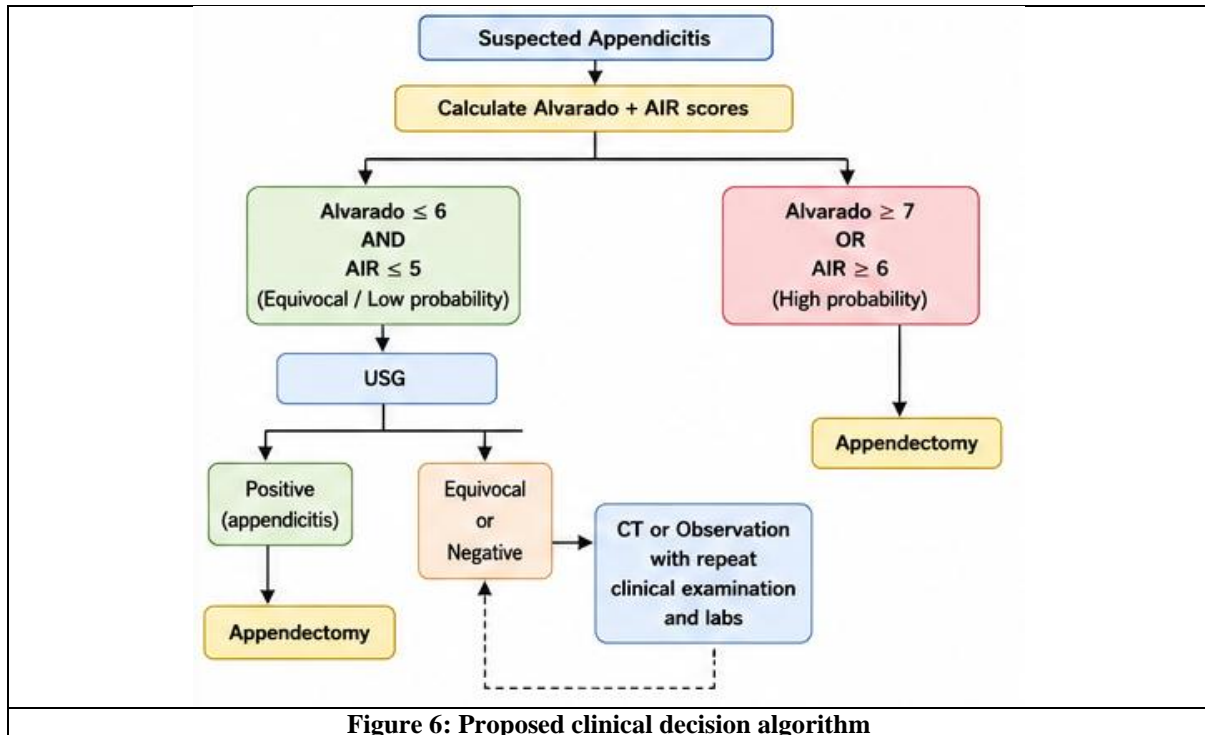


Figure 6: Proposed clinical decision algorithm

Study limitations should be acknowledged. The retrospective study design naturally carries risks of selection and incomplete data bias. The five negative appendectomy cases are few in absolute number to permit proper multivariable logistic regression, and in fact limit statistical power analysis of subgroups. CT scan data was not available in a formal manner across the entire study cohort and could not be included as a predictor variable. Symptoms duration, BMI, or specific clinical signs such as Rovsing's or psoas sign were not present in all the records we were able to retrieve and could not be analysed. We feel that our study still enjoyed some strength of design in its consecutive cohort design, with histopathologic verification as the outcome “gold standard” in all cases, and sample size which met a priori specified target for n. Stronger studies, they are, would exist of standardised data collection, systematic CT use and multivariate analysis to generate robust knowledge of independent predictors.

CONCLUSION

A negative appendectomy rate of 2.27% observed across 220 consecutive appendectomies over thirty-six months reflects a high standard of diagnostic accuracy at this institution. Low Alvarado score (≤ 6), low AIR score (≤ 5), near-normal total leucocyte count, mild or absent neutrophilia, CRP below 20 mg/L, and negative or equivocal ultrasonography are the strongest measurable correlates of histologically normal appendix in this cohort. These parameters are individually and collectively available at the point of clinical assessment and do not require advanced imaging. A

standardised pre-operative checklist incorporating mandatory cross-sectional imaging for patients with any combination of these findings—rather than relying solely on clinical gestalt—offers a practical and evidence-based strategy to eliminate residual negative appendectomies without compromising timely intervention in high-probability cases.

Declarations

Funding: This research received no external funding.

Conflicts of Interest: The authors declare no conflicts of interest pertaining to this work.

Ethics Approval: Approval was obtained from the Institutional Ethics Committee, Indira Medical College and Hospitals. A waiver of informed consent was granted in view of the retrospective, minimal-risk study design.

Data Availability: Anonymised data supporting the findings of this study are available on reasonable request to the corresponding author.

Author Contributions: C.M.: study concept, data collection, statistical analysis, manuscript preparation. V.P.: Data collection, patient record review, interpretation of results, critical revision of manuscript. M.F.: histopathological analysis, critical revision of the manuscript. All authors reviewed and approved the final version.

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