Original Article

The Accuracy Of [1]upper Gastro- Ntestinal Endoscopy Versus Histology And [2] The Tests For H.pylori Diagnosis

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Abstract

OBJECTIVES :Due to the prevelance of H.pylori in the governorate ,the study aimed to determine :1-the accuracy of endoscopy in the diagnosis of chronic upper gastro-intestinal pathologies ,in comparison with accuracy of their histologic diagnoses .

2- the accuracy of the tests for detection of H pylori ,and to compare them with each other .

SETTING:

Salahuddin Governorate , Tikrit City, Tikrit General Hospital [T.G.H.] ,to the north of Baghdad ,Iraq.

PATIENTS AND METHODS : Over 8 months ,seven biopsies were harvested from intact areas of gastric antral mucosa , duodenal bulb , gastric body and lower third of oesophagus of each one of 200 patients undergoing oesophago-gastro-duodenoscopy in the hospital. The biopsies were submitted for histopathological, cultural and biochemical investigations. All patients ,pooled from various districts of the governorate ,gave written consents. The basic statistical analyses were applied to the results of endoscopy and tests for H.pylori detection.

RESULTS :

A: We determined the accuracy rates of endoscopy in detecting upper gastr-intestinal lesions ,and compared them with the accuracy rates of histopathological examinations of the same lesions ,which were regarded as the reference with which to compare

B : We identified accuracy rates of the histopathology of biopsies to detect H.pylori ,and compared them with the accuracy rates of culture and urease test of the same biopsies to detect the same bacterium .

CONCLUSIONS

1- The histological diagnosis is the gold standard for the diagnosis of H.pylori infection.

2- The endoscopy has a high specificity ,moderate sesitivity ,in detecting upper gastro-intestinal lesions .

3- The tests applied for detection of H.pylori have high sensitivity and specifity.

Key Words: Tikrit, Gastritis, duodenal lesions , oesophagitis, H.pylori, , sensitivity ,specificity, positive predictive value ,negative predictive value , test accuracy ,accuracy rate .

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Introduction

Before embarking on the statistical analysis , simple basic statistical defininitions are important ,followed by suggested hints from our side to help memorize these definitions . Accuracy of a test is its correspondance with the true value.[1] ,while the Precision of a test is its reproducibility when repeated on the same sample[1] ,and under the same clinical , enviromental ,and laboratory conditions .These definitions , are based on the fact that each test ,formulated to discover a disease ,when applied to the patient ,will end in either POSITIVE or NEGATIVE result .Equivocal results will ultimately prove to be either positive or negative .Each one of these in turn could either be TRUE or FALSE.

The properties of useful diagnostic tests , canbe summerized as such [1]

:1 Test methodology is well-described and is reliably reproducible.

2-A reference range has been established

.3-The sensitivity and specificity of the test has been reliably established by comparison with a gold standard ,likewise for accuracy and precision of the test .

Based on these assumptions ,the following statistical tools have been recognised :

$$\text{1-Sensitivity} = \frac{\text{True positive}}{\text{True positive} + \text{False negative}} \times 100$$

It is the ability of the test to show evidence of a disease in all of those patients who do have that disease.It is the complement of false negative [ie, false negative rate plus sensitivity equalls 100%] [2]. The less the false negative results are ,[i.e. approaching zero] ,the hgher the sensitivity is going to be [i.e. apporaching 100%] [1-5].

$$\text{2- Specificity} = \frac{\text{True negative}}{\text{True negative} + \text{false positive}} \times 100$$

It is the ability of the test to exclude a disease in all of those patients who actually do not have it [1-5].It is the complement of false positive [ie, false positive rate plus specificity equalls 100%][2] .The less the false positive results are going to be [i.e.,appraching zero],the more the specificity is going to be [i.e. ,appraoching 100%] The sensitivity and specificity are determined in relation to a gold standard test ,ie,a reference test with which they are compared..It is test that has been thoroughly evaluated and which has a minimum of false positive and false negative results .[1,2,6-9] .However sometimes it is difficult to determine the gold standard test for an illness [pancreatitis]

$$\text{3- Positive predictive value} = \frac{\text{True positive}}{\text{True positive} + \text{false positive}} \times 100$$

It is the ability of the test to predict the disease in those patients with positive test results . Simply it is the percentage of true positve resuls to the total of all positive results [1,3,4,]. If false positive results number approaches zero, then

the positive predictive value will be greater and approaches 100 %. This test is also called a Posttest probability after a positive test [1] . When the false negative value and the false positive value are numerically the same , the sensitivity will be equall to positive predictive value

$$4\text{- Negative predictive value} = \frac{\text{True negative}}{\text{True negative + False negative}} \times 100$$

It is the ability of the test to predict absence of the disease in those patients who have negative test results .Simply it is the percentage of true negative results to the total of negative results [1,3,4].If the false negative results number approaches

zero , then the negative predictive value would be approaching 100%. When the false negative value and the false positive value are numerically the same , the specificity will be equall to negative predictive value .

$$5\text{-Accuracy rate} = \frac{\text{True positive + True negative}}{\text{Total}} \times 100$$

It is an indicator of how accurate the test is , when applied to patients with or without the disease for which it was formulated to identify [4] . To enlarge about this test , the following possibilities are considered :

A The figure of [True positive] ,may either become higher and higher enough to approach the [Total],and hence the figure of [True negative]will be smaller and smaller till it reaches zero ,and the accuracy rate will be approaching 100%, where it wil

l be regarded as a confirmatory test [An example are the confirmatory tests of hepatitis virology] .B-The reverse may happen ,and the figure of [True negative] will be higher and higher , so as to approach the [Total] ,and the figure of [True positive]will be smaller and smaller to approach zero , where the accuracy rate, again will be almost 100%, so the test will become a test of exclusion .

It is important to diffientiate between accuracy [already defined] and accuracy rate as already stated .

Patients, materials, and methods Sample Size :

Usually endoscopy is carried out for an average of 12 patients per week; that is around 624 patients per year. Hence 200 patients would constitute around 32% of this total. Hence it is found to be a representative figure of the whole patients attending endoscopy unit of the hospital. Over an eight-month period, every third patient endoscoped was randomly chosen to be involved in the study.

The study protocol It was approved by the departments of microbiology and medicine, and the local ethical committee in the hospital. The study is an analytical, and a descriptive one.

The study extended over the period from November 1999 through June 2000. This hospital is secondary care ,400-bedded hospital, and is the main city and governorate hospital. It serves more than 1 million population. Patients attending it belong to various socio-economic classes and occupations.

According to a questionnaire format, each patient was asked in detail about his symptoms, previous endoscopy, x-rays, past medical history, drugs and family history. The instrument used was Olympus GIF Q20 fiberoptic gastroduodenoscope, with two biopsy forceps labelled 1 and 2. The endoscope was sterilized after each procedure. The forceps were disinfected with 70% ethyl alcohol for 10 minutes, and then washed with normal saline after each use. The light source was Olympus SLE, and a double-chambered vacuum sucker was used. The patients were fasting overnight. No sedation was given. A consent was obtained from each patient, written down in the case notes. Seven biopsies were obtained from each patient, two antral biopsies within 2cm from pylorus [one for histopathology, the second for microbiology (urease test and culture)]. Likewise, two duodenal biopsies from the 1st part of duodenum, and also 2 oesophageal biopsies from the lower third of the oesophagus, were managed in the same way as antral biopsies. One biopsy was obtained from stomach body, sent for histopathology (10). The biopsy specimens were transported to bacteriology laboratory by sterile 2 ml tube containing brain heart infusion broth. They were kept at 40 c until processing. Processing was carried out usually 1 3 hours post biopsy (11,12). For microbiological purposes, each biopsy specimen was minced with sterile disposable surgical blade in sterile petri dish under sterile conditions. One piece was handled by sterile loop and inoculated a solid medium for culture.

Another part was handled by another sterile loop and inoculated in urea slant for direct urease test. The rest of the specimen was used for Gram stain.

Three types of solid culture media were used (11,12)

1.Brain heart infusion agar with 5 7% human blood

2.Blood agar base No 2 with 5 -7% human blood

3.Muller Hinton Agar with 5 7% human blood

All were supplemented with vancomycin 6mg/lit, Nalidixic acid 20 mg/lit and Griseofulvin 2 mg/lit to avoid contamination (11,12). The inoculated plates were kept in a Co2 jar with gas generating kit, liberating 8% O2, 5 8% Co2 and 80% H2 (micro-aerophilic condition) and were left for 5 7 days at 370 in the incubator. They were examined for H.pylori colonies after this period. After inoculation of the minced specimen in urea slant, the time was recorded for any change in colour to develop (red), and reported as the following: within 10 minutes, within 20 minutes, within one hour, within 2 hours, within 3 hours, overnight, and up to 24 hours. The tubes were kept in the incubator at 370

c.Gram stained slides were examined for gram-negative spiral bacteria. To confirm the diagnosis, from each positive culture plate, a small number of colonies was tested by Gram's stain, urease test, oxidase test and catalase test.

The histological biopsies were processed routinely and were stained with Heamatoxylin Eosin and Giemsa stains. The 1st stain was utilized to show histological changes and to show H.pylori , the second to show H.pylori.

Criteria for inclusion

:1.Patients with recurrent or chronic symptoms (i.e. > three months)

.2.Only the patients who were referred by their caring physicians, were involved in order to avoid self-reporting of acute upper gastro-intestinal symptoms that may be caused by viruses (hepatitis), bacterial infections (food poisoning) or drug intolerance

Criteria for exclusion:

Patients were excluded from the study when

:1.Antibiotic or bismuth or antisecretory compounds have been used over the last two weeks

.2.There was a major gastro-intestinal surgery recently.

3.There was evidence of major organ ure (heart,

brain, liver, and kidneys).

disease or failure (heart, brain, liver, and kidneys).

4.The patient was less than fourteen years old

5.There was an acute gastrointestinal emergency (bleeding, persistent vomiting or diarrhoea or pain)

.6.Previous endoscopy within the study period

.7.Pregnancy.

Statistical Methods

:1. The accuracy tests were calculated according to the known formulae

.2. All the results were handled and tabulated by the computer

.Criteria of endoscopic diagnoses of(13):

1-. Gastritis: Endoscopico examination describes the visible changes of gastric mucosal lining such as oedema, erythema, friability, exudates, flat erosions, nodularity, raised erosions, rugal hyperplasia, rugal atrophy, visibility of vascular pattern, and in tramural bleeding .Topographically, gastritis is divided into gastritis of antrum (type B), pangastritis (antrum predominant or corpus predominant) or gastritis of corpus (type A) .corpus (type A) .

2. Oesophagitis: Oedema, erythema, exudates and erosions were utilized to diagnose oesophagitis .The extent of the findings were utilized to determine the grade of inflammation.

3. Duodenitis: Same gross features as in No 2were utilized to diagnose duodenitis .

4. Ulcer: Whether oesophageal, gastric or duodenal is obviously the mucosal discontinuity with which the base is deep and the margin is surrounded by oedema and erythema.

Results

I-The diagnosis of upper GIT lesions :

A-Endoscopy

A1 : The endoscopy of the stomach lesions [mainly gastritis] :

Sensitivity= 36.2%.

Specificity= 100 [no false positive results (endoscopy positive, histology negative). Same applies for positive predictive value]

Positive predictive value=100 %

Negative predictive value =44.5 %

Accuracy rate: = 59%.

A2:The endoscopy of duodenal lesions [duodenitis and duodenal ulcer] :

The sensitivity = 95 %

The specificity = 100% [there are no false positive results, (i.e., endoscopy positive, but histology is negative). The same applies for positive predictive value.]

The positive predictive value = 100%

The negative predictive value = 98 %

The accuracy rate = 99 %.

Almost similar results are gained when the equations were applied to the figures of [Duodenal ulkers] and [Duodenitis] seperately .Therefore the results were gathered together as [Duodenal Lesions].

A3: The endoscopy of the oesophageal lesions [mainly oesophagitis] :

The sensitivity=77.6%

The specificity= 100%

The positive predictive value = 100%

The negative predictive value = 89.9%

B : The histology of upper GIT lesions :

B 1:The histology of the stomach lesions [Gastritis]:

The sensitivity= 100%

The specificity= 100%

The positive predictive value = 100%

The negative predictive value = 100%

The accuracy rate =100%

B2 :The histology of duodenal lesions [total of both duodenal ulcers and duodenitis]

The sensitivity= 100%

The specificity=100%

The positive predictive value =100% \

The accuracy rate =100%

B3: The histology of oesophageal lesions [mainly oesophagitis] :

The sensitivity =100%

The specificity =100%

The positive predictive value = 100%

The negative predictive value = 100%

The accuracy rate =100%

II-The diagnosis of H.pylori [in antral biopsies

In order to ease comparison ,each statstical tool figures are determinened for various diagnostic tests following each other .

The sensitivity of histopathology= 100%

The sensitivity of culture = 81 %.

The sensitivity of urease test = 89 %

The specificity of histopathology= 00%

The specificity of culture= 94.2%

The specificity of urease test= 100%

Positive predictive value of histopathology =100%

Positive predictive value of culture =100 %

Positive predictive value of urease test =100%

Negative predictive value of histopathology= 100%

Negative predictive value of culture =78 %

Negative predictive value of urease test = 91 %

Acuracy rate of histopathology= 100%

Acuracy rate of culture = 86.5%

Accuracy rate of urease test= 94.5 %

Discussion

A-The accuracy of endoscopy versus histology:

Basically the histology was given a score of 100% in all statistical tools ,which make it the gold standard for the detection of various GIT lesions .The low sensitivity of endoscopy in detection of gastritis[36.2%] may be explained by the fact that mild gastritis may

be bypassed by the endoscopist as normal, as usually in this situation, there will be only erythema, which maybe regarded a normality. The criteria of moderate to severe gastritis are already clear [13], that can be hardly missed. Therefore it maybe stated that a biopsy should be harvested from antrum and body of an allegedly [normal stomach], for histological diagnosis, as there m

ay actually be a mild form of gastiritis ,especially in symptomatic patients.It is obvious that the endocopy is far much less sensitive than histology[gold standard test] in detection of gastritis The positive predictive value for endoscopy is maximum [ie ,100%] „this is because the endoscopy is just simply telling us a lesion is there when it clear for the naked eye ., while the negative predictive value is low [44.5%] , as the endoscopycannot

exclude a dignosis when it is not visible [or not clear] to the naked eye .For these reasons the accuracy rate of endoscopyis low as well [59%] But the endoscopic method for diagnosis of duodenal lesions had almost same sensitivity rates as histologic diagnosis (95% and 100% respectively). The endoscopy has got high figures for the rest of the statistical tools in this aspect as well ,for it seems that duodenal lesions are usually clear,from the outset,to the naked eye . When there is duodenitis ,the area of involvement will be clear and can be differentiated from the rest of the duodenum , not as it is in the stomach where the normal erythema is

already diffuse . Un ulcer ,wherever it is ,can hardlybe missed .The rest of the tools showed high figures as well .[99-100%] . The moderate sensitivity of endoscopy in detection of osophagitis {60% in one study[I],while our figure for the same was 77.6%} may suggest that when symptoms are suggestive of oesophagitis or gastro-osophageal reflux, it is better always to proceed for osophageal biopsy sent for histology even when oesophagus looks normal endoscopically. The sensitivity of endoscopy in detection of oesophagitis is far less than that of the histology ,probably for the same reasons already stated ..The figures for the rest of the statiscal tools were comparatively high [comparing endoscopy to histology] .The oesophageal ulcer can hardly be missed

.Table no.1 summerizes the findings of our study.

B-The accuracy of H. pylori diagnosis tests:

Some investigators have found that the overall sensitivity ,specicificity ,positive prdictive value and negative predictive value have a figure of > 90 % ,for the tests detecting H.pylori [5] C13 urea breath test ,histopathology ,and CLO test are the gold standard tests for the detection of H.pylori[5,6].Other investigators add PCR and serology to the armamentorium of the diagnosis of H.pylori ,[8] but regard the culture as the gold standard test .However serlogy has a low sensitivity and specificity , while H.pylori stool antigaen detection test has a high sensitivity and specificity ,and is a good alternative for monitering response to therapy of H.pylori.[8] .Other investigators regard culture of H.pylori as unrelible and regard CLO test as a cheaper and a more sensitive test than other biopsy based tests [9] . In our study , we have utilized the prolonged urease test,as was followed by other investigators [5]], and which has showed a sensitivity of 89% .The rest of the figures for this prolonged ureases test varied between 90-100% in our study .However we did not utilise UBT test ,nor stool antigen,or PCR in our study .

It is evident from the figures showen in the comparison table no. 2 , that histopathology[which gave a score of 100% in all aspects] is superior to culture in the detection of H.pylori in gastric biopsies.

The sensitivity of histopathology is almost comparable to the widely utilized urease slide test. It is to be stressed again that minute numbers of H.pylori in the biopsy specimens may not be regrown on culture plates, for many reasons, some of which are the small number of organism, the patchy distribution of H.pylori in gastric mucosa, and past usage of antisecretory , antibiotics or proton pump inhibitors ,which were not declared by the patient. The same applies for urease slide test[CLO test] ,which has in the opinion of some investigators a sensitivity of 95 %,same for culture as well.[7].

Experience has shown that small numbers of H.pylori, however, can be seen in histology specimen. Therefore the histopathological examination to detect H.pylori may be superior to culture in gastric biopsies. Based on this, it could be regarded as the reference test for the detection of H.pylori, with which ,other tests are going to be compared. In the hands of an experienced pathologist, a colony of H.pylori, cannot be a false positive, but the interpretation of the colony by the microbiologist may be inaccurate, the thing which may have happenned in our study ,likewise colonies of other contaminants may be misinterpreted as H.pylori ..This conclusion may be strengthened further by the fact that the some oesophageal and duodenal biopsy specimens ,when subjected to histological examination ,showed very low frequency of H.pylori detection, as it happened in our study as well .This conclusion runs in line with other studies .

Again it is clear that antrum constitutes the most frequent site of colonization in the stomach [9], (detected by histology mainly) followed by the oesophagus ,followed by duodenum .Hence histology may be superior to culture for detection of H.pylori infection from the antrum, but culture may be identical to histopathology in detecting the infection from oesophagus and duodenum. The reason for that could be the minute number of H.pylori bacteria residing in the oesophagi and duodena. Stomach body was not cultured [9] .See table no 2 for comparison of various tests However still many investigaters recommend a combination of 2 tests ,in order to increases the sensitivity of detection of H.pylori.[5] ,and the combination of CLO,histology and culture reveal a sensitivity of 94 % and specificity of 88% .[5]

suggestions

In ordere to help memorize these statistical tools ,the following hints are suggested on our side :

1-Sensitivity : True positiveness,which is repeated twice in the equation , is associated with presence of disease .

2-Specificity True negativeness , which is repeated twice in the equation ,is associated with absence of the disease.

3-Positive predictive value : All positives on either side of the equation ,[may be compared with sensitivity] .

4-Negative predictive value : All negatives on either side of the equation,[may be compared with specificity .]

5 - Accuracy rate: This test takes into consideration only true results , and it is the only one as such. .Likewise it is the only test that utilizes the[Total] as a denominator.

Conflicts of Interest : none is there

Table no.1 .Comparison Between Statistical Tools Ap plied to U pper GIT Endoscopy Findings versus those Applied to Histology Findings .

Test	Statistical tool	Gastritis	Duodenal lesions	Osophagitis
OGD	Sensitivity %	36.2	95	77.6
	Specificity %	100	100	100
	Positive P.V *.%	100	100	100
	Negative P.V *.%	44.5	98	89.9
	Negative P.V *.%	44.5	98	89.9
	Acc** .Rate %	59	99	92.5
Histology	Sensitivity %	100	100	100
	Specificity %	100	100	100
	Positive P.V *.%	100	100	100
	Negative P.V *.%	100	100	100
	Acc** .rate %	100	100	100

* :Predictive Value

** :accuracy

Table no.2. Comparison Betweeen Statistical Analysis Tools Applied to H.pylori Diagnostic Tests in Five Studies .

Test	Stat. tool	Current Study	Ref.* 5	Ref.* 6	Ref.* 7	Ref.*9
Histology	Sn**	100	77			91
	Sp***	100				92
	PPV****	100				
	NPV*****	100				
	AR	100				
CLO test	Sn**	-			90	92
	Sp***	-			98	92
	PPV****	-				
	NPV*****	-				
	AR	-				
UBT	Sn**	-	90	90		92
	Sp***	-	90	95		92
	PPV****	-	90			
	NPV*****	-	90			
	AR	-	90			
Culture	Sn**	81				85
	Sp***	94				97
	PPV****	100				
	NPV*****	78				
	AR	86				
Urease test	Sn**	89				
	Sp***	100				
	PPV****	100				
	NPV*****	91				
	AR	94				

Legend :* :reference,**:sensitivity,***:specificity,****:positive predictive value ,
***** negative predictive valuecuracy rate ,Stat.=statistical ,
UBT :urea breath test

Table (3): Age and Sex Distribution of the Examined Patients.

Age Group (Year)	No. of Males	No. of Females	No of Total	Percentage (Out of total)	H.pylori. Positive patients* (No %)
14 to 19	2	13	15	7.5	6 (40)
20 to 29	24	21	45	22.5	19 (42.2)
30 to 39	17	25	42	21	18 (42.8)
40 to 49	19	21	40	20	21 (52.5)
50 to 59	16	17	33	16.5	20 (60.6)
60 to 69	5	13	18	9	13 (72.22)
70 to 79	4	1	5	2.5	4 (80)
80 to 89	1	0	1	0.5	1 (100)
90 to 99	0	0	0	0	0 (0)
100 to 109	0	1	1	0.5	1 (100)
Total	88	112	200	100	103 (51.5)

* By any mean .

Table No.4 Ⅲ.Upper GIT Endoscopy Findings versus Histology Findings

Histological Diagnoses	Source of biopsies	Total No. of [biopsies]	No. of positive endoscopic diagnoses [%]	No. of positive Histologic Diagnoses [%]
Gastritis	Gastric antrum	192	46 [23]	127 [63.5]
Duodenal lesions	1st Part of duodenum	200	92[46]	94[47]
Oesophagea l lesions	Lower 1/3 of oesophagus	200	52 [26]	67 [33.5]

Tp=true positive , Tn =true negative ,Fp= false positive ,Fn=false negative .

Gastritis : Tp=127 ,Tn=192-127=65 ,Fp =zero ,Fn =zero

Duodenal lesions :Tp=92,Tn=200-94=106 ,Fp=zero ,Fn =94-92=2

Oesophageal lesions : Tp=67 ,Tn =200-67=133 ,Fp=zero ,Fn =67-52=15

Table No.5 : Comparison between Positive Tests for H.pylori Diagnosis in the Current Study .

Source of biopsy	No. of patients [biopsies]	No. of Positive cultures for H.pylori [%]	No. of positive histopathologies for H.pylori [%]	Positive urease tests no.[%]
Stomach	200	76 [38]	103 [51.5]	92[46]

Legend : Tp=True positive Tn=true negative,Fp=False positive ,Fn=False negative,

For histopathology :Tp=103, Tn=200-103=97 ,Fp=0 ,Fn=0

For urease tests :Tp=92 ,Tn=200-103= 97 ,Fp=0 ,Fn=103-92=11

For culture Tp=76 ,Tn=200-103=97 , Fp=0, Fn=103-76=27

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