

Evaluating diagnostic significance of magnifying narrow band imaging endoscopy in various gastric lesions

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Abstract: Background: Narrow-band imaging (NBI) is a novel endoscopic technique that may enhance the accuracy of diagnosis by using narrow-bandwidth filters in a red-green-blue (R/G/B) sequential illumination system. In the current study we try to evaluate the diagnostic significance of magnifying narrow band imaging endoscopy in various gastric lesions, this may provide an early diagnosis of malignant and premalignant changes of the mucosa with enhanced selection of appropriate treatment, as gastric malignancy is one of the most common malignant tumors, and is the second commonest cause of cancer deaths worldwide. **Methods:** The current study included 101 patients whose upper gastrointestinal endoscopy showed different gastric lesions not in active bleeding and those patients were reevaluated by using magnifying narrow band imaging technique. Biopsies were taken from these target lesions for histopathological examinations. The presence of gastric carcinoma and high grade intraepithelial neoplasia in the biopsy samples was considered as a positive pathological result, which is used to assess the accuracy of endoscopic diagnosis. **Results:** There were differences in the accuracy, sensitivity, specificity, PPV and NPV of the magnifying narrow band imaging (ME-NBI) endoscopy in detecting presence of dysplasia or neoplasia in different gastric lesions. With overall sensitivity 63.6% which is superior to that of conventional white light imaging (C-WLI) endoscopy (36.3%). **Conclusion:** Magnifying NBI is more sensitive than conventional white light endoscopy in detection of high grade dysplasia and early gastric cancer in different gastric lesions. But, still ME-NBI endoscopy is not sufficient to replace conventional histopathology.

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1.Introduction

Gastric lesions are identified by changes in color and irregularity of surface mucosa in endoscopic examination. Recent advances in technology enable us to obtain more detailed information during endoscopic procedures in order to provide an early diagnosis of malignant and premalignant changes of the mucosa with enhanced selection of appropriate treatments.

Narrow-band imaging (NBI) is a novel endoscopic technique that may enhance the accuracy of diagnosis by using narrow-bandwidth filters in a red-green-blue (R/G/B) sequential illumination system (13). The depth of penetration into the mucosa depends on the wavelength used, superficial for the blue band, deep for the red band and intermediate for the green band. This results in visualization of the vascular network and surface texture of the mucosa in an effort to improve tissue characterization, differentiation, and diagnosis in different inflammatory and neoplastic (pre-malignant and malignant) lesions (10). The magnified NBI technique paid attention to both micro vascular (MV) and micro surface (MS) pattern changes and thereafter proposed the vessel plus surface (VS)

classification, this classification categorized MV and MS pattern separately into three types, namely, regular, irregular, absent and set criteria for gastric cancer as "presence of an irregular MV pattern with a demarcation line" or "presence of an irregular MS pattern with a demarcation line" (14).

2. Patients and Methods:

The current study was done at the endoscopy unit of Ain Shams University Hospital, Cairo, Egypt. During the period from January 2010 till July 2012 the study was approved by the hospital ethical committee and included 101 patients complaining of upper abdominal dyspepsia. The patients had first given a written informed consent for study participation. Clinical examination was done to all patients, those patients whose upper gastrointestinal endoscopy showed different gastric lesions and not in active bleeding, they underwent endoscopic examination using the magnifying NBI endoscopy (PENTAX EPK-I) in order to determine the pit pattern and vascular patterns of these lesions according to the "vessel plus surface (VS) classification system (5). Endoscopic mucosal changes were found in some patients; in the form of

gastritis, ulcers, polyps, or masses. Multiple biopsies were taken from the edges and the base in case of ulcers, small polyps were resected, wide based large polyps and masses were biopsied and then biopsies were fixed in 10% formalin, routinely processed, and embedded in paraffin blocks. 5 um thick sections were cut on glass slides and stained with haematoxylin and eosin. The slides were examined by a pathologist who was unaware of the nature of the endoscopic diagnosis and it was found that The histopathological examination revealed that hyperplastic polyps were the most common among other polyps (62.5%) which was in accordance with a study of **KeKilli et al** (7) who studied 124 cases; 55.6% of them were with polyps of hyperplastic type.

Moreover adenocarcinoma was the most common among other invasive malignancies (44%) which was in agree with **Esmaili et al** (3), although they represented a higher ratio than our study; 275 cases of upper gastrointestinal malignancy; 97.8% of whom were conventional adenocarcinoma. This might be due to the difference in the study design as they focused mainly on the cases of invasive malignancy, as well as greater number of the studied patients.

Such classification system used to determine micro vascular pattern and micro surface pattern by the vessel plus surface (VS) classification system included, Regular micro vascular pattern (RMVP) and Irregular micro vascular pattern (IMVP). While the micro surface pattern (MS) included, regular micro surface pattern (RMSP), Irregular micro surface pattern (IMSP) and absent micro surface pattern (AMSP). The Vessel plus surface classification system differentiate between the noncarcinomatous and carcinomatous lesions including the high grade dysplasia (HGD) and early carcinoma (EC) in the gastrointestinal tract as follow:

	Non carcinoma	HGD or EC
MV architecture	RMVP	IMVP
MS structure	RMSP	IMSP

As regards the histopathological examination, the presence of gastric carcinoma and high grade intraepithelial neoplasia in the biopsy samples was considered as a positive pathological result, which is used to assess the accuracy of endoscopic diagnosis.

The results were statistically analyzed using the Statistical Package for Social Sciences (SPSS version 18). The sensitivity (Sn), specificity (Sp), positive predictive value (PPV), Negative Predictive Value (NPV) and accuracy of magnifying NBI endoscopy in different gastric lesions were calculated with reference to the histopathological diagnosis.

3. Results:

The current study included 101 patients (54 males and 47 females) above the age of 18 years old. Presented with abdominal dyspepsia and their conventional upper gastrointestinal endoscopy showed different gastric lesions as shown in Table (1).

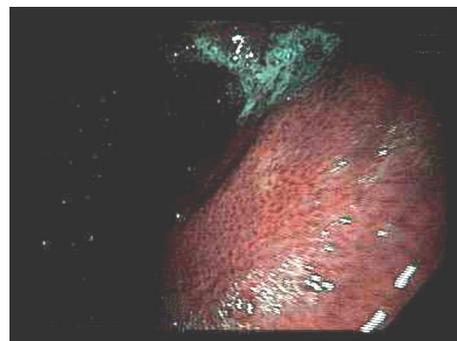
Table (1): Number and percentage of different gastric lesions in the current study by conventional light endoscopy

Light endoscopy		
	N	%
Ulcer	6	5.94
Ulcer + Gastritis	14	13.86
Polyp + Gastritis	16	15.84
Mass	7	6.93
Polyp	16	15.84
Gastritis	42	41.58
Total	101	100.00

The total number of cases with ulcer either alone or associated with gastritis was 20 cases, the number of cases with pypoidal lesion either alone or associated with gastritis was 32 cases. The total number of cases with gastritis either alone or associated with ulcer or polyp was 72 cases and the total number of cases with mass lesion was 7.



(A)



(B)

Figure (1): Pan gastritis; by conventional light endoscopy (A) and by NBI (B) shows round pit pattern and regular SECN.

As regards NBI findings in cases of gastritis;

On application of magnifying narrow band imaging endoscopy (M-NBI) to these lesions, we detected 5 cases out of 42 cases of pure gastritis proved by conventional light imaging endoscopy (C-WLI), having suspicion of dysplasia with IMSP and IMVP. However, the other lesions of gastritis either associated with polyps or ulcers showed no suspicion of dysplasia by M-NBI (fig.1).

As regards the histopathology of the 5 cases with high suspicion of HGD or EC by M-NBI, only one case proved to have gastritis with areas of high grade dysplasia, while, the other 4 cases have gastritis only without any dysplasia or malignant changes. However, in the cases showed no suspicion of dysplasia by M-NBI, the histopathology showed one case having dysplasia. As shown in table (2).

Table (2): The relation between the NBI findings and the histopathological findings in cases of gastritis as regard the detection of dysplasia or early carcinoma

NBI (G)		Histopathology		
		Negative for dysplasia or EC	Positive for dysplasia or EC	Total
Negative for dysplasia or EC	N	66	1	67
	%	91.67	1.39	93.06
Positive for dysplasia or EC	N	4	1	5
	%	5.56	1.39	6.94
Total	N	70	2	72
	%	97.22	2.78	100.00
Sens.	Spec.	PPV	NPV	Accuracy
50.00	94.29	20.00	98.51	93.06

PPV: positive predictive value NPV: negative predictive value

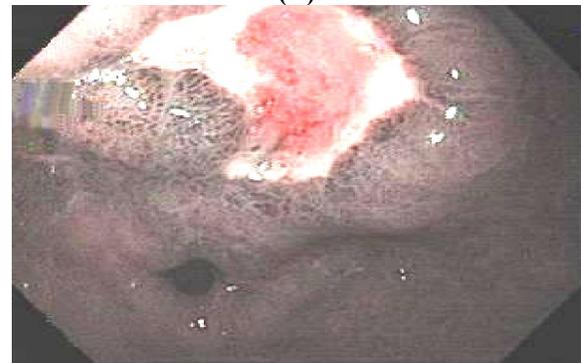
Form this table, we can see that, the accuracy of M-NBI endoscopy in detection of dysplasia or early carcinoma in cases with gastritis is 93.06 % and has a good specificity and negative predictive value (94.29% and 98.51% respectively) with low sensitivity and positive predictive value (50 % and 20% respectively).

As regards NBI findings in cases of ulcers;

By conventional light endoscopy there were 20 cases of ulcer lesions, two of them suspected to have malignant changes. Whereas, with application of the magnifying NBI technique, There were 4 cases with ulcer lesion showing areas of (IMSP) and (IMVP) suggesting the presence of high grade dysplasia (HGD) or early carcinoma (EC) including one of the two cases suspected by conventional light endoscopy. As regards the histopathology of the 4 cases with high suspicion of HGD or EC by M-NBI, only one case proved to have areas of high grade dysplasia While the other 3 cases showed presence of mononuclear inflammatory cells and neutrophils and neither atrophy nor dysplasia, however, in the cases showed no suspicion of dysplasia by M-NBI, the histopathology showed one case having dysplasia. As shown in table (3).



(A)



(B)

Figure (2): A prepyloric ulcer; by conventional light endoscopy (A) and by NBI (B), the ulcer edge shows round to oval pit pattern and regular SECN

Table (3): The relation between the NBI findings and the histopathological findings in cases with ulcer as regard the detection of dysplasia or early carcinoma

NBI (U)		Histopathology		
		Negative for dysplasia or EC	Positive for dysplasia or EC	Total
Negative for dysplasia or EC	N	15	1	16
	%	75.00	5.00	80.00
Positive for dysplasia or EC	N	3	1	4
	%	15.00	5.00	20.00
Total	N	18	2	20
	%	90.00	10.00	100.00
Sens.	Spec.	PPV	NPV	Accuracy
50.000	83.333	25.000	93.750	80.000

From this table, we can see that, the accuracy of M-NBI endoscopy in detection of dysplasia or early carcinoma in cases with ulcers is 80 % and has a good specificity and negative predictive value (83.33% and 93.75 % respectively) with low sensitivity and positive predictive value (50 % and 25 % respectively).

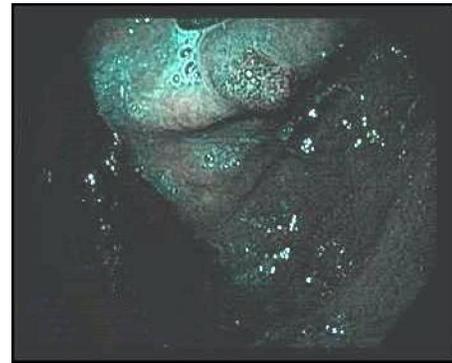
As regards NBI findings in cases of polyps;

On application of magnifying narrow band imaging endoscopy (M-NBI) to these lesions, we detected 4 cases having suspicion of dysplasia with IMSP and IMVP, However, the other lesions of polyps showed no suspicion of dysplasia by M-NBI (fig.3). As regards the histopathology of the 4 cases with high suspicion of HGD or EC by M-NBI, only

one case proved to have areas of high grade dysplasia, while the other 3 cases revealed presence of inflammatory cells with no metaplasia or dysplasia, however, in the cases showed no suspicion of dysplasia by M-NBI, the histopathology showed one case having reactive atypia and high grade dysplasia. As shown in table (4).



(A)



(B)

Figure (3): Fundic gastric polyp; by conventional light endoscopy (A) and by NBI (B), the polyp shows round pit pattern and regular SECN**Table (4): The relation between the NBI findings and the histopathological findings in cases with polyp as regard the detection of dysplasia or early carcinoma**

NBI (P)		Histopathology		
		Negative for dysplasia or EC	Positive for dysplasia or EC C	Total
Negative for dysplasia or EC	N	27	1	28
	%	84.38	3.13	87.50
Positive for dysplasia or EC	N	3	1	4
	%	9.38	3.13	12.50
Total	N	30	2	32
	%	93.75	6.25	100.00
Sens.	Spec.	PPV	NPV	Accuracy
50.000	90.000	25.000	96.429	87.500

Form this table, we can see that, the accuracy of M-NBI endoscopy in detection of dysplasia or early carcinoma in cases with polyps is 87.5 % and has a good specificity and negative predictive value (90 % and 96.42 % respectively) with low sensitivity and positive predictive value (50 % and 25 % respectively).

As regards NBI findings in cases of masses:

By conventional light endoscopy there were 7 cases of mass lesion, 4 of them suspected to have gastric neoplasia. Whereas, with application of the magnifying NBI technique there were 5 cases (including 3 cases suspected by light endoscopy) highly suggestive of gastric neoplasia (fig. 4). While, the other cases showed no suspicion of dysplasia with RMSP and RMVP.

As regards the histopathology of the 5 cases with high suspicion of HGD or EC by M-NBI, there was

an infiltrate extending through muscularis mucosa to submucosa composed of malignant large round cells exhibiting fairly dense chromatin in 4 cases. While the 5th case showed marked infiltration of mononuclear inflammatory cells and neutrophils and neither atrophy nor dysplasia. However, in the other 2 cases showed no suspicion of dysplasia by M-NBI, the histopathology showed presence of malignant large round cells exhibiting fairly dense chromatin in one of them, while the other one does not exhibit any dysplasia or cellular atypia; as shown in table (5).

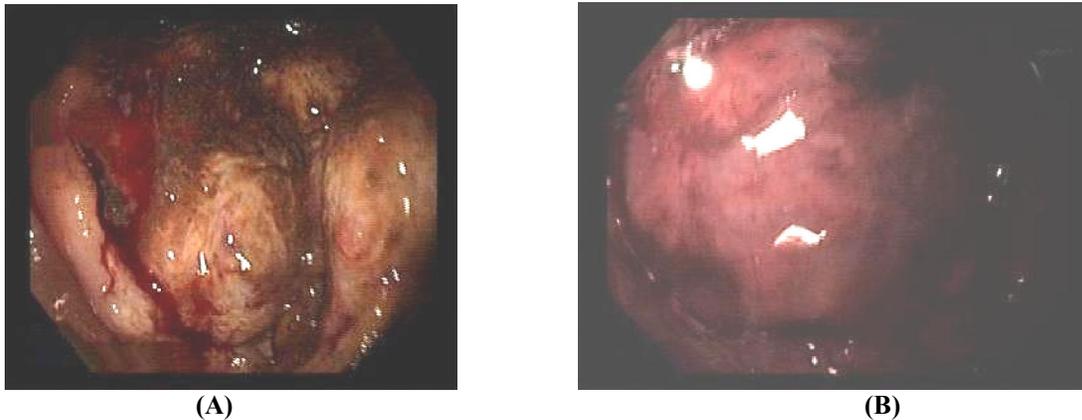


Figure (4): Gastric mass; by conventional light endoscopy (A) and by NBI (B) showed absent MS and distorted MV pattern

Table (5): The relation between the NBI findings and the histopathological findings in cases with gastric mass as regards the detection of dysplasia or early carcinoma

NBI (M)		Histopathology		
		Negative for dysplasia or EC	Positive for dysplasia or EC	Total
Negative for dysplasia or EC	N	1	1	2
	%	14.29	14.29	28.57
Positive for dysplasia or EC	N	1	4	5
	%	14.29	57.14	71.43
Total	N	2	5	7
	%	28.57	71.43	100.00
Sens.	Spec.	PPV	NPV	Accuracy
80.000	50.000	80.000	50.000	71.429

Form this table, we can see that, the accuracy of M-NBI endoscopy in detection of dysplasia or early carcinoma in cases with mass lesion is 71.49 % with sensitivity, specificity, PPV and NPV about (80%, 50%, 80% and 50% respectively).

As regard detection of dysplasia or EC by conventional light endoscopy in different gastric lesions, there was only 6 suspected to have malignancy (4 cases with mass lesions and 2 cases with ulcer lesion) and only 4 cases proved to have

malignancy by histopathology (3 masses and one ulcer). Whereas, no cases with gastritis or polyp lesions were suspected to have malignant changes as shown in Table (6).

Table (6): The relation between the Light endoscopy findings and histopathology in different gastric lesions as regards the detection of dysplasia or malignancy.

Light endoscopy		Histopathology		
		NO	YES	Total
Negative	N	88	7	95
	%	87.13	6.93	94.06
Positive	N	2	4	6
	%	1.98	3.96	5.94
Total	N	90	11	101
	%	89.11	10.89	100.00
Sens.	Spec.	PPV	NPV	Accuracy
36.364	97.778	66.667	92.632	91.089

From this table, we can see that, the accuracy of the Light endoscopy in detection of dysplasia or early carcinoma in different gastric lesions is 91% with specificity 97.778 % and negative predictive value 92.6%. But the sensitivity and positive predictive value are 36.36% and 66.6% which are low.

As regard detection of dysplasia or EC by M-NBI endoscopy in different gastric lesions, there was 15 cases showed IMSP and IMVP, picture suggestive for presence of dysplasia or neoplasia and this was confirmed by histopathology in 7 cases only, while the

Other 8 cases showed neither dysplasia nor neoplasia. Whereas, in the other 86 cases showed no suspicion of dysplasia by M-NBI, the histopathology detected the presence of dysplasia in 4 cases; as shown in Table (7).

Table (7): The relation between the NBI findings and the histopathological findings in different gastric lesions as regards the detection of dysplasia or early carcinoma

NBI		Histopathology		
		Negative for dysplasia or EC	Positive for dysplasia or EC	Total
Negative for dysplasia or EC	N	82	4	86
	%	81.19	3.96	85.15
Positive for dysplasia or EC	N	8	7	15
	%	7.92	6.93	14.85
Total	N	90	11	101
	%	89.11	10.89	100.00
Sens.	Spec.	PPV	NPV	Accuracy
63.636	91.111	46.667	95.349	88.119

From this table, the accuracy of M-NBI endoscopy in detection of dysplasia or early carcinoma in different gastric lesions is 88.1% with specificity 95.3% and negative predictive value 95.34%. But the sensitivity and positive predictive value are 63.6% and 46.66%; which are low.

There was difference in the sensitivity, specificity, PPV and NPV of the magnifying NBI endoscopy in detecting presence of dysplasia or

neoplasia in depressed and elevated gastric lesions; Table (8).

Table (8): The sensitivity, specificity, PPV and NPV of the magnifying NBI endoscopy in detecting presence of dysplasia or neoplasia in depressed and elevated gastric lesions

NBI	Sens.	Spec.	PPV	NPV
NBI in flat and depressed lesions (gastritis+ulcer)	50 %	92.045 %	22.22 %	97.59 %
NBI in elevated gastric lesions (polyps+masses)	71.42 %	87.5 %	55.55 %	93.33 %

There was difference in the accuracy, sensitivity, specificity, PPV and NPV of the magnifying NBI endoscopy in detecting presence of dysplasia or neoplasia in different gastric lesions. As shown in table (9).

Table (9): The accuracy, sensitivity, specificity, PPV and NPV of the magnifying NBI endoscopy in detecting presence of dysplasia or neoplasia in different gastric lesions

	Sens.	Spec.	PPV	NPV	Accuracy
Mass	80.000	50.000	80.000	50.000	71.429
Ulcer	50.000	83.333	25.000	93.750	80.000
Polyp	50.000	90.000	25.000	96.429	87.500
Gastritis	33.333	93.056	16.667	97.101	90.667

4. Discussion

Narrow-band imaging (NBI) is a novel endoscopic technique that may enhance the accuracy of diagnosis by using narrow-bandwidth filters in a red-green-blue (R/G/B) sequential illumination system (13).

In the current study we try to evaluate the diagnostic significance of magnifying narrow band imaging endoscopy in various gastric lesions and this may provide an early diagnosis of malignant and premalignant changes of the mucosa with enhanced selection of appropriate treatment, as gastric malignancy is one of the most common malignant tumors, and is the second commonest cause of cancer deaths worldwide (12).

The magnified NBI technique paid attention to both micro vascular (MV) and micro surface (MS) pattern changes and thereafter proposed the Vessel plus Surface (VS) classification. This classification categorized MV and MS pattern separately into three types, namely, regular, irregular, and absent and set criteria for gastric cancer as "presence of an irregular MV pattern with a demarcation line" or "presence of an irregular MS pattern with a demarcation line" (16). The current study was conducted on 101 patients (54 males and 47 females) above the age of 18 years old. Whose conventional upper gastrointestinal endoscopy showed different gastric lesions, they were followed by ME- NBI endoscopy examination to clarify the value of such new technique. As regards the flat and depressed gastric lesions (gastritis and ulcer), the current study revealed that the ME- NBI endoscopy is superior to conventional white light imaging endoscopy in detection of dysplasia or early carcinoma, with ME-NBI sensitivity, specificity, PPV, NPV and accuracy in gastritis are 50%, 94.29%, 20%, 98.5% and 93.06% respectively and in ulcer lesions are 50%, 83.3%, 25%, 93.75% and 80% respectively. With overall sensitivity and specificity of ME-NBI in flat and depressed gastric lesions are 50% and 92% respectively. This matches with the results of the study done by **Kaise et al (4)** on 100 images of superficial gastric depressions (55 depressed cancers, 45 benign depressions) with sensitivity and specificity as follow, (72%, 80%) for ME-NBI and

(71%, 65%) for C- WLE, with ME-NBI diagnosis superior to C-WLI endoscopy. As regards elevated gastric lesions (polyps and masses), the current study revealed that the ME- NBI endoscopy is superior to conventional white light imaging endoscopy in detection of dysplasia or early carcinoma With ME-NBI sensitivity, specificity, PPV, NPV and accuracy in polyps are 50%, 90%, 25%, 96.4% and 87.5% respectively and in mass lesions are 80%, 50%, 80%, 50% and 71.49% respectively. With overall sensitivity and specificity of ME-NBI in elevated gastric lesions are 71.4% and 87.5% respectively. And this matches with the results of the study done by- **Miwa et al (10)** who did a retrospective, comparative study on 135 patients with elevated and depressed gastric lesions and the sensitivity and specificity in elevated lesions showed that ME-NBI is more diagnostic than C- WLI with sensitivity 82.4 versus 70.6% and specificity 97.3 versus 54.7%.

With referral to the overall sensitivity of the magnifying NBI endoscopy (63.63%) compared to that of conventional white light imaging endoscopy (36.36%) in different gastric lesions either elevated or depressed, we found that, the magnifying narrow band imaging endoscopy is more sensitive than the conventional white light imaging endoscopy and is useful in differentiating the pathology of focal gastric mucosal lesions. And this matches with the results of **Ang et al (1)** who said that ME-NBI is useful in differentiating the pathology of focal gastric mucosal lesions than the conventional white light endoscopy through a study was done on 458 Chinese patients. Also, we agree with the result that was done by **Kato et al (6)** who found that, ME-NBI achieved superior accuracy in the differential diagnosis of superficial gastric lesions identified with C-WLE through a prospective, comparative study done on 201 lesions from 111 patients who had a high risk of gastric cancer. And also, the result of the study done by **Capelle et al (2)** who said that ME-NBI compared to routine C-WLE increases the diagnostic yield for detection of advanced premalignant gastric lesions through a study done on patients with previously identified gastric intestinal metaplasia or dysplasia underwent a surveillance endoscopy.

As regards the micro surface and micro vascular patterns, we found that, the regular micro surface pattern (RMSP) and the regular microvascular pattern (RMVP) are consistent with benign lesions, while, the IMSP, AMSP and IMVP are consistent with presence of high grade dysplasia (HGD) or carcinoma. These ME-NBI findings matches with the findings in the study done by **Maki et al (9)** where they defined the endoscopic criteria for early cancer as an irregular microvascular pattern with a demarcation line, or irregular microsurface pattern with a demarcation line, using ME-NBI through a study done on 93 consecutive superficial elevated lesions of the stomach .Also, These ME-NBI findings matches with the results of the studies done by **Zhang et al (15) and Kenshi et al (8)** Where **Zhang et al (15)** showed presence of irregular minute vessels and variation in the caliber of vessels in cases diagnosed as early gastric cancer or precancerous gastric lesions and **Kenshi et al, 2002** revealed a regular sub epithelial capillary network in noncancerous mucosa. While in all carcinomas, the regular capillary pattern of noncancerous mucosa had disappeared and irregular micro vessels were proliferating.

In our study there were 15 patients with NBI findings suggesting presence of dysplasia or EC, but the histopathology confirms the diagnosis in 7 cases only. Also the histopathology detected another 4 cases with dysplasia neither detected by C-WLE nor magnifying NBI. With low sensitivity 63.6% of the ME-NBI in detection of dysplasia or EC. And this matches with the result of the prospective study done by **Nakayoshi et al (11)** Who studied the correlation between the magnified images obtained with the NBI system and the histological findings and concluded that magnifying NBI endoscopies are not sufficient to replace conventional histopathology.

Conclusion:

Magnifying NBI is more sensitive than conventional white light endoscopy in detection of high grade dysplasia and early gastric cancer in different gastric lesions. But, still ME-NBI endoscopy not sufficient to replace conventional histopathology.

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