REVIEW OF CALINCLOPATHOLOGY OF GASTRIC
BIOPSY IN KTH BETWEEN 2008-2010.

By

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A thesis submitted in parietal fulfillment for requirement of degree of clinical MD in pathology in October 2010

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بِسْمِ اللَّهِ رَحْمَتَكِ ۝ رَحْمَةَ الۢوَلِيدَاتِ ۝ رَحْمَةَ النَّاسِ
# CONTENT

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dedication</td>
<td>I</td>
</tr>
<tr>
<td>Acknowledgment</td>
<td>II</td>
</tr>
<tr>
<td>List of abbreviation</td>
<td>III</td>
</tr>
<tr>
<td>English abstract</td>
<td>IV</td>
</tr>
<tr>
<td>Arabic abstract</td>
<td>VI</td>
</tr>
<tr>
<td>List of figures</td>
<td>VII</td>
</tr>
<tr>
<td><strong>Chapter One</strong></td>
<td></td>
</tr>
<tr>
<td>1.1. Literature Review</td>
<td>1</td>
</tr>
<tr>
<td>1.2. Normal anatomy &amp; histology of stomach</td>
<td>6</td>
</tr>
<tr>
<td>1.3. Handling of gastric biopsy</td>
<td>17</td>
</tr>
<tr>
<td>1.4. Benign gastric lesion diagnosis by endoscopy</td>
<td>30</td>
</tr>
<tr>
<td>1.5. OBJECTIVES</td>
<td>33</td>
</tr>
<tr>
<td><strong>Chapter Two</strong></td>
<td></td>
</tr>
<tr>
<td>Methodology</td>
<td>34</td>
</tr>
</tbody>
</table>

**Chapter One**

1.1. Literature Review

1.2. Normal anatomy & histology of stomach

1.3. Handling of gastric biopsy.

1.4. Benign gastric lesion diagnosis by endoscopy

1.5. OBJECTIVES

**Chapter Two**

Methodology
<table>
<thead>
<tr>
<th>Chapter Three</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Results</td>
<td>36</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Chapter Four</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>4.1.Discussion</td>
<td>52</td>
</tr>
<tr>
<td>4.2.Conclusion</td>
<td>55</td>
</tr>
<tr>
<td>4.3. Recommendations</td>
<td>56</td>
</tr>
<tr>
<td>REFERENCES.</td>
<td>57</td>
</tr>
</tbody>
</table>
Dedication

I dedicate this effort to the loving memory to my father,

mother, they devoted their live to proper educational

upbringing of their eight children.

Acknowledgment

I would like to thank all who share me ideas, advice and

encouragement.
First of all, I want to thank all patients who suffer a lot from these lesions. I am grateful to my supervisor Dr Mohammed Othman for co-operative supervision. Great thank to my brothers and only one sister those help me much.

I would like to thank Dr Alnazer Mohammed, Dr Babker Ishage, Dr Othman ALjrafy, and Dr Amar Hassan, for acceptance to review their case.

Thank also extended for all staff member in histology department in KTH for their co-operation.
ABSTRACT

Gastric biopsy can provide a diagnosis & direct therapy. These biopsies are obtained by inserting an endoscope into the oropharynx and passing it through the esophagus and into the stomach. Forceps are threaded through the endoscope, and pieces of tissue are obtained for microscopic examination. Most commonly, biopsies are targeted at the visualized abnormality, although in some instances random sample is performed, particularly in the setting of non-healing ulceration. A diagnostic gastric biopsy can generate information regarding gastritis, gastropathy, vascular lesions, and neoplasia.

This is a retrospective study conducted in Sudanese patients attended to gastric endoscopic unit in the KTH between January 2008- January 2010.

The study objective is to review clinical-pathological these biopsy, to determine the endoscopic finding and their anatomical locations.

The study is conducted to 100 patients, 49% are female and 51% are male. Microscopic examination of the slides (formalin fixed, paraffin wax embedded, H&E, and Gemsiea stains) revealed that.
The most common benign gastric lesion that diagnosed are gastritis with H. pylori microorganism association with phenotype of severe form, gastric polyps, and peptic ulcer disease.

These benign gastric lesions are mostly located in antrum and fundus part of the stomach and commonly associated with endoscopic gastric mucosal abnormality such as ulcers.

- The distribution among the young adult with slightly male predominance.

- Most malignant lesion are adenocarcinoma are located in pyloric region of stomach, and the endoscopic finding are mass or mucosal ulcer, the age distributions are old age group.

Absence of clinical input, adequate sampling, and proper labeling, lead to descriptive non diagnostic interpretations, false negative or positive diagnosis, and misclassifications, so good communication between the gastroenterologist and pathologist are need in the future studies.
ملخص الطرح

دخول منظار المعدة ادي الى تحسين في تشخيص وعلاج الأمراض التي تصيب المعدة. يتم ادخال المنظار عن طريق اعلي البلعوم والمري وصولا الى المعدة ومن اخذ عينة من الابراج المصابه يهدف المنظار الى تشخيص حالات مثل التهابات الغشاء المخاطي، الاوعي الدمويه والاورام.

هذه دراسة استقصائية اجربة اجريت علي مرضى يعانون من اعراض امراض معوية تم اخذ عينات من المعدة، بلغ عدد المرضى مائة مريض حوالي واحد وخمسين من الذكور وتسعة واربعون من الإناث من مختلف الفئات العمرية في الفترة ما بين يناير 2010 وحتى يناير 2011.

أوضح الدراسة ان معظم الحالات التي تم تشخيصها هي التهابات المعدة. دوالي المعدة، قرح المعدة بالإضافة الى سرطان المعدة.

أوضح الفحص النسبي أن معظم اسباب التهاب المعدة المدمن هي بكتريا حلزونية. يكثر نموها في الجزء القاعي والأمامي من المعدة مع وجود التهابات جادة واخري مزمنه معظم الفئات العمرية ما بين اربعين إلى اربعين سنة.

معظم حالات سرطان المعدة تقع في الجزء العلوي من المعدة وتظهر عن طريق المنظار في شكل اورام أو قرح. معظم اعمار المرضى ما بين الستون والثمانون سنة.
أوضح خلاصة الدراسة عدم وجود بيانات كافية عن الفحوصات السريرية والمتعلقة الخاصة بالمرضى مع عدم اتخاذ كافية من أجزاء مختلفة من المعدة ادي إلى عدم اكتمال تشخيص بعض الحالات.
1. LITERATURE REVIEWS

1.1. Normal Histology of Stomach

The Stomach develops from the distal part of the foregut. it is a
secular organ with volume of 1200 to 1500 ml , but capacity of over 3000
ml. it extend from just left of the midline where it connect to the
duodenum . The duodenum the concavity of the right, inner curve, the in-
cisura angularis, marks the approximate point at which the stomach
narrow prior to its junction with the duodenum. The entire stomach is
covered by peritoneum an-exaggerated peritoneal fold, the greater
omentum; extend beyond the great or curvature to transverse colon.

The stomach divided into five anatomic regain, the cardia, is
narrow antral portion of stomach immediaty distal to gastroesophgeal
junction. The fundus is dome – shaped portion of proximal stomach that
extend supero-lateral to gastroesophageal junction. The body or corpus
comprises the remainder of the stomach proximal to incisura angularis.
The stomach distal to this angle is the antrum, demarcated from the
duodenum by the muscular pyloric sphincter.

The gastric wall, like the vast of gastrointestinal tract, consist of
mucosa, muscular is propria and seroa. The interior surface of stomach
exhibits coarse rugae (meaning folds). These enfolding  of mucosa and
sub-mucosa extend longitudinally and are most prominent in proximal of stomach, flattening out when stomach is distended. A finer mosaic – like pattern is delineated by mucosal gland. The normal gastric mucosa has two compartments: the superficial foveolar (meaning leaf-like) compartment and deeper glandular compartment. The foveolar compartment is relatively uniform through the stomach. In contrast, the glandular composition exhibits major difference in the thickness and in glandular composition in the different regions of the stomach. The foveolar compartment consist of surface epithelial cells (the foveolar cells) lining the entire mucosal surface as well as the gastric pits. The lush undulation of the mucosal surface and pits impart the leaf like texture to gastric mucosa, the tall, columnar mucin – secreting foveolar cells have basal nuclei and crowded, small, relatively clear mucin – containing extremely common in these regions as the entire gastric mucosal surface is totally replaced every 2 to 6 days. The glandular compartment consists of gastric glands, which very between anatomic regions:

- Cardia glands contain mucus – secreting cells only.
- Oxyntic cells called gastric of fundic glands are found in the fundus and body and contain parietal cells chief cells and scattered endocrine cells .the term oxyntic means acid forming.
• Antral or pyloric glands-contain mucus-secreting cell and endocrine cells.

The main cells types in these glands are the following:

• Mucous cells populate the glands of cardia and antral regions and secrete mucus and pepsinogen.

• Partial cells line predominantly, the upper half of oxyntic gland in the fundus and body. They are recognized by their bright eosinophilia on H&E stained preparation which is attributable to their abundant mitochondria. The apical membrane of the parietal cells is invaginated, forming an extensive intercellular canalicular system complete with microvillus. In the resting state, vesicle lies in close approximation to the canalicular system. These vesicles contain the proton pump, a unique hydrogen–potassium-ATPase (H, K-ATPase) that pump hydrogen across membranes in exchange for potassium ions. Within minutes of parietal cells stimulation, the vesicles fuse with the canalicular system, thereby creating an-apically directed acid-secreting membrane of enormous surface area, parietal cells also secrete intrinsic factor, which binds luminal vitamins B12 in the duodenum and permits its absorption in the ileum.
Chief cells concentrated more at base of gastric glands are responsible for the secretion of proteolytic proenzyme pepsinogen (I and II). Chief cells are notable for their basophilic cytoplasm, and ultrastructurally are classic protein synthesis cells having an extrusive rough endoplasmic reticulum / prominent supra-annular Golgi apparatus’ and numerous apical secretary granules’ - upon stimulation of chief cells the pepsinogen contained in granules are released by exocytosis the pepsinogen are activate to pepsin by low luminal PH and inactivate above PH 6 upon entry in the duodenum.

Endocrine cells are scattered among the epithelial cells of gastric and antral glands. The cytoplasm of these triangular cells contain small brightly eosionophilic granules, which are concentrated on the basal aspect of the cells. These cells can act in an endocrine mode, releasing their products into circulation, or apoacrine mode via secretion into the basal tissue. In the antral mucosa most of the endocrine cells are the gastrin – producing cells or G cells. In the body (gastric) mucosa, the endocrine cells produce histamine, which bind the histamine – (H2) receptor on partial cells to increase acid production (ECL) cells. Other ECL cells in the gastric mucosa include O cells producing somatostain and X
cells (producing endothelin) these cells play important role in modulate acid production.

1.2. Gastric mucosal physiology:

1.2.1 Acid secretion:

The hallmark of gastric physiology is secretion of hydrochloric acid, divided into the three phases.

- The cephalic, initiated by the sight, taste, smell, chewing and swallowing of palatable food, is mediated by vagal activity.

- The gastric phase involves stimulation of stretch receptors by gastric distention and is mediated by vagal impulse; it also involves gastrin release form endocrine cells, the G cells, in the antral glands. Gastrin release is promoted by luminal amino acids and peptides and possibly by vagal stimulation.

- The intestinal phase, initiated when food containing digested protein enters the proximal small intestines, involves a number of polypeptides besides gastrin.

All signals converge on the gastric parietal cells to activate the proton pump:
_Acetylcholine_ released form cephalic –vagal afferent stimulates the parietal cell via the muscarine-3-cholinergic receptor, resulting in an in cytosolic Ca and subsequent activation of the proton pump.

_Gastrin activates a gastrin receptor, resulting an increase of cytosolic Ca within the parietal cells._

_An oxyntic gland ECL cells plays a central role; gastrin and vagal afferents induce the release of histamine form the ECL cells , thereby stimulating the H receptor on parietal cells . This pathway is considered to be the most important for activation of proton pump._

Activation of some receptor on the parietal cells surface inhibits acids production. They include receptors for somatostatin, prostaglandin of E series, and epidermal growth factors.

1.2.2.MUCOSAL PROTECTION:

At maximal secretary rate the intra-luminal concentration of hydrogen ions is 3 million times greater than that of the blood and tissues. The mucosal barrier protects the gastric mucosa form auto-digestion and consist of:

_Mucus secretion: The thin layer of surface mucus in the stomach and duodenum exhibits a diffusion coefficient for H that is one quarter that of water. Acid –and pepsin-containing fluids exists the gastric glands as_
jets passing through the surface mucus layer, entering the lumen directly
without contacting surface epithelial cells.

_Bicarbonate secretion:_ surface epithelial cells in both the stomach and
duodenum secrete bicarbonate into the boundary zone of adherent mucus,
creating an essentially PH neutral microenvironment immediately
adjacent to the cell surface.

_The epithelial barrier:_ intercellular tight junctions provide a barrier to
back-diffusion of hydrogen ions. Epithelial disruption is followed rapidly
by restitution, in which existing cells migrate along the exposed
basement membrane to fill in the defects and restore epithelial barrier
integrity.

_Mucosal blood flow:_ The rich mucosal blood supply provides oxygen,
bicarbonate, and nutrients to epithelial cells and removes back-diffused
acid.

_Prostaglandin blood flow:_ Production of prostaglandin by mucosal cells
impacts on many other component of other component of mucosal
defense. For example, prostaglandin favor production of mucus and
bicarbonates, and they inhibit acid secretion by parietal cells .In addition,
by vaso-dilatory action, prostaglandin E and I improve mucosal blood
flow. Drug that blocks prostaglandin synthesis reduce this cyto-protection and thus promote gastric mucosal injury and ulceration.

When the mucosal barrier is breached, the muscularis mucosa limits injury. Superficial damage limited to mucosa can heal within hours and to days. When damage extends into the sub mucosa, weeks are required for complete healing. Imperfect as our understanding of these defensive mechanisms may be, they are clearly a physiologic marvel, or our gastric walls would suffer the same fate as a piece of swallowed meat.

In addition to the well-characterized barrier function and digestive functions of the gastric mucosa, mucosal endocrine cells also produce hormones that are involved in growth regulation. Ghrelin is a recently identified growth hormone that regulates body growth hormone that regulates body growth and appetite via a possible effect on the gastrointestinal- hypothalamic- pituitary axis.

1.3. Handling of gastric biopsy:

Gastric biopsies can provide useful information beyond the identification of inflammation or Helicobacter organism. The key to maximizing the diagnostic yield is providing sufficient context adequate and good communication clinical information including medical history surg-gical procedure , endoscopic impression , and imaging finding aids in
detection and classify of finding. Adequate biopsies entail good sampling technique, proper labeling and submission. Histological evaluation can be enhancing by special stain, ancillary studies and working knowledge of the diversity of diagnosis. Difficult cases are best managed by a combined clinico-pathologic approach.

Gastric biopsy can provide diagnosis and direct therapy. These biopsy are obtain by inserting an-endoscopic into the oro-pharynx and passing it through the esophagus, and piece of tissue are obtained for microscope examination, most common biopsies are targeted at a visualized abnormality although in some intense random sampling is preformed, particularly in the setting of anon healing ulceration. A diagnostic gastric biopsy can generate information gastritis, gasteropathy, vascular lesion, neoplasia or structural abnormality. However, the absence of valuable clinical input, adequate sampling and proper labeling lead to description non-diagnostic interpretation, false negative or positive diagnosis and misclassification (ie reduce sensitivity and specificity).

1.3.1 Clinical Information:

All gastric biopsy need to be accompanied by appropriate clinical information to obtain a complete history, the clinical reforming the patient to the gastroenterologist should provide complete information and that history should be submitted to the pathologist. These include not only
medical and surgical history but also patient family history and know ingestion of non-steroidal anti-inflammatory drugs, iron and other potential toxic substance, particularly important medical history includes information regarding systemic disease, immune-compromise, cirrhosis or history of cancer. Histroy of transplantation can be aid in the recognition of gastric – graft versus – host disease as one study showed a false – negative and false- positive interpretation in 27% and 36% re-spectively, of cases subjected to blind review. History can also provoke special stain for protein deposition such as myeloid immune-histochemical stains for occult neoplastic infiltrates.

1.3.2. Endoscopic and Imaging Information

Endoscopic impression as well as information available through other imaging modalities is likewise extremely important location, distribution and physical configuration of lesional tissue are all attribute that should be available to the pathologist. Vascular lesion is better observed and classified at time of endoscopy rather than at histologic review. Distinction of a Cameron erosion, prolapsing fold, angiodysplasia, and Dieulafoy"s lesion is the province of gastroenterologist rather the pathologist.

In addition, problem with sampling error resulting in false-negative biopsies for gastric carcinoma can be mitigated by astute clinical
observation. A recent study examined endoscopic detection of gastric adeno-carcinoma and found a false-negative rate of 22% (28/129). In the case in which either the pathologist or gastroenterologist deemed the biopsy inadequate or findings suspicious, there was a median delay of 12.2 days between the false negative and true positive study. However, in those 18% (14/129) cases in which the pathology was interpreted as negative and symptom were attributed to benign pathology, the median interval was 3 weeks.

1.3.3. Tissue Sampling & adequacy:

The adequacy of tissue sampling depend on the biopsy forceps, operator technique, visibility of lesions and tissue handling. Both the 2.8 mm and 3.6 mm channel biopsy with obtain tissue of similar depth, although the latter yield 2-3 times, the surface area. Generally full – thickness biopsies are obtain without much sub mucosa, although the sample is more superficial when taking biopsy from greater curvature of the body or in the context of hypertrophic gasteropathy. Superficial samples pose particular problem when trying to identify a deep mucosal/sub mucosal lesion or accurately assess gastric biopsy. Endoscopic ultrasound guided true – cut biopsy can be used to obtain deeper sample of gastric wall and might be particularly help full to diagnose suspected
gastric carcinoma or gastro intestinal stromal tumor\(^6\). In case of suspected lymphoma obtain fresh tissue for flow cytometry analysis

1.3.4. Tissue Acquisition

Technical considerations include method of manipulating forceps and handling the tissue. Exerting pressure against the wall as one applies the open forceps can result in a shallower biopsy, where snapping back quickly after it is closed on the pressure can create crush artifact, both impediments to diagnostic interpretations. Likewise, care has to be extracting tissue from the tissue forceps. Pushing the tissue form base of forceps with a blunt probe is preferable to pushing form the top, which can squash the tissue or shaking tissue form instrument, which can denude the surface epithelium. Taking a double bite (ie, 2 mucosal biopsies) with a single pass of endoscope, although efficient, has potential problem of small sample (<2 mm) and tissue loss, particularly when using forceps without a spike. One study, tissue loss was seen 9 times more frequently with a 2-bite compared with 1-bite technique\(^7\).

1.3.5 Tissue Submission

Another means for avoiding tissue loss is to submit on more than 4 tissue fragment in a single container of formalin. The more pieces submitted and the more variability in size, the less the likelihood that tissue
fragment will be oriented in same plane when embedded in paraffin and sectioned evenly when creating a glass slide for histologic review. Ideally, the number of pieces submitted in a given container should be specified on requisition sheet, so that the laboratory can verify all material is received and reviewed.

**1.3.5. Proper labeling:**

It is important to avoid placing samples from different area or lesion in same vial. This practice obscures the difference among the different type of gastritis and under-mines the intent of mapping. Gastritis is best defined not by describing the finding in the singles pieces of tissue but rather by the assessment topography include the location, the depth and focality of inflammation, metaplasia, and atrophy, this possibility only when multiple biopsies are obtained from different regions of stomach. The Sydney system and its modifications, the most widely used classification of gastritis recommended biopsy specimen to be obtain the greater and lesser curvature of proximal body, and lesser curvatures at incisura angularis. This approach enables the distinction between antral predominant non atrophic gastritis, non atrophic pan-gastritis, and antrum restricted atrophic gastritis, and cuprous predominant atrophic gastritis, multifocal atrophic gastritis and atrophic pan-gastritis. The caveat mapping the stomach is not as easy feat for the gastroenterologist. In one
study 2 experienced gastroenterologists were asked to obtain 7 biopsies in a specified order; this goal was achieved only in 33% of the cases\textsuperscript{10}. However, the ability to accurately diagnoses atrophy and dysplasia by using only the first 3 biopsies was 78% and 33% respectively, compared with the diagnoses rendered after review all 7 biopsies.

At a minimum 1-3 biopsy properly labeled and separately submitted form antrum and the body are required for correct classification of gastritis. Recently a grading and staging system that score inflammation and atrophy receptively, on basis of distributions of change in the antrum and body has recommended\textsuperscript{11}.

The pathologist ability to distinguish an antrum form body biopsy might be lost with wide spread metaplasia. Despite to adequate sample, inadequate labeling leads to a descriptive diagnosis noting the presence of inflammation and metaplasia but providing no insight as to disease pathogenesis progression, neoplastic risk, or associated disease processes. This ultimalty lead to poor patient are, predominant gastritis and hypochlorhydria or achlorhydria who is maintained on proton pump inhibitor as result of the diagnosis of "active chronic gastritis " and reflux type symptoms ,a patient with carcinoid tumor who undergo gastric resection appropriate to a sporadic but an autoimmune- associated lesion
as result of failure to identify the back ground of predominant gastritis and a patient with marked gastric atrophy who does not undergo sufficient surveillance for the detection of the associated dysplasia and carcinoma.

In addition, proper labeling can enable the gastroenterologist and surgeon to return to the site of lesional tissue. Approximately 20% of gastric carcinoma and lymphomas are Borrmann type 0, which is either superficial protruding or non protruding lesion. These lesions can be difficult to locate a second time of initial endoscopy, a number of stomach irregularities were noted and biopsied. However, a repeat biopsy might be necessary if the initial sample is in conclusive. In addition, the cancer must be localized for surgical management.

The reasoning behind placing several samples produced by multiple passes into a single container is to reduce costs to the patient. However this compromise is neither good patient care cost-effective if the net result is additional testing to provide an accurate diagnosis. Furthermore, the cost advantage is minimal at best. However, if multiple diagnoses are rendered, the pathologist should bill a professional fee per diagnosis. Thus there is minimal financial gain and possibility of substantial loss of information to be afforded by this practice.

1.3.6. Tissue processing and slide staining:
The microscopic is dependent not only on the endoscopic skills in obtaining an adequate sample in terms of sized or number of biopsy sample but also on sufficient thin sections to make the necessary observation. Typically 2 to 3 mm thick piece of tissue. Thus, there must be representative levels going is not missed. Most laboratories routinely meet this standard; however, periodically problem can be rise such as malfunction of processer or training of new technication that lead to sub-optimal material for diagnostic evaluation. Most laboratories use as H&E staining for routine evaluation; whoever, additional stain can be helpful in detection of both organism and extracellular deposit.(see table 1)

1.3.7.Histological evaluation:

The pathologist approaches biopsies by scanning the slide with low power objective to establish how many pieces of tissue are present and whether there is obvious area of disease. The type of gastric mucosa is determined on the base of label provided and the architecture and glandular cells composition of tissue. Alteration of normal pit-glands architecture including erosion, ulcer, foveolar hyperplasia, tortuosity, increased glands or glandular dropout, cystic dilation, and presence of intestinal metaplaisa can be rapidly observed. The epithelium is scrutinized to distinguish normal form reactive and dysplastic/ neoplastic. In addition pigment deposit, apoptosis of epithelium or increase number
of mitotic figure with altered form of diagnostic clues. The lamina propria is examined for inflammatory and neoplastic infiltrate, fibrosis, and muscular strand, extracellular deposit and altered blood vessels. In addition to luminal aspect of the biopsies is examined, iron crystal or exogenous material that may play an etiological role in the tissue injury. Common diagnoses and key finding are shown in Table 2.

1.3.7. Correlation between Histologic and endoscopic finding:

Concordance between the endoscopic finding and histological finding is present in two third or less of case even when the endoscopic observation and mild gastritis is classified as normal and the question is reduced to presence or absence of gastritis\(^{15}\). Interestingly, even in case of endoscopically classified erosive gastritis, the biopsy might show normal finding. This most likely represents a sampling effect in part. Lack of agreement is seen in both body and antrum biopsies.

The problem is not unique to adult but is also seen in the pediatric population.\(^{16}\) This known discrepancy should precluded any management or study observation on patient mode solely on basis of endoscopic classifications.

1.4. Benign gastric lesion that diagnosis by endoscopy:

1.4.1. Gastritis:
The incidence and natural history of chronic gastritis has been clarified by systematic use of endoscopic gastric biopsy. The two main features of this disease are infiltration of lamina propria by inflammatory cells and atrophy of glandular epithelium. The plasma cells and lymphocytes (with occasional formation of follicles) predominate among the inflammatory cells, but eosinophils and neutrophils may also be present. If inflammatory infiltrate are limited to the foveolar region and accompanied by glandular atrophy, the condensation is designated as chorionic superficial gastritis. Subtle epithelial abnormalities seen in this form include a reduction of cytoplasmic mucin, nuclear and nuclear enlargement, and some increase of foveolar mitoses. When the inflammations become extensive and accompanied by glandular atrophy, the condition is termed chorionic atrophic gastritis, and is further categorized as mild, moderate, or severe by roughly estimating the thickness of glandular portion of whole mucosa. Naturally, properly orientated mucosa is needed to make this estimation. Glandular atrophy is also manifested by increase in distance between the gland and condensation of reticulin fibers in lamina propria. If thin of mucosa is seen without inflammatory change, the condition is designated as gastric atrophy, acknowledging the fact that in most cases this properly represent the end stage of a chronic atrophic gastritis. Increasing degree of atrophy are commonly associated with cystic dilation of gland and metaplasia. In rare
case of autoimmune gastritis, the atrophy may have patchy quality, resulting in pseudopolypoid and appearance of oxyntic mucosa.

Two type of metaplastic change can occur in chronic gastritis, often in combination: pyloric metaplasia of the fundic mucosa and intestinal metaplasia.

In pyloric metaplasia, there is replacement of the fundic type glands by mucin secreting glands. This is gradual process that proceeds as front along the fundic –pyloric junctions and move proximally toward the cardiac. In intestinal metaplasia refer to the progressive replacement of gastric mucosa by epithelium having light electron microscopic feature of intestinal epitheliums of either large bowel type, including goblet cells, absorptive (brush border) cells, panth cells and varity of endocrine cells. Intestinal al metaplasia has further divided in to complete (type1) and in complete (type2). In complete metaplasia, the gastric mucosa changes to a pattern identical to that of small bowel epithelium with development of vili and crypt in most case. In in-complete metaplasia, absorptive cells are absent, where columnar cells with the appearance of gastric foveolar cells are retained.

The relationship between intestinal metaplasia of stomach and Helicobacter pylori is interest. H- Pylori usually absent in intestinal metaplasia type 1 but usually present in foci of type 2; ie, those in which
some gastric feature are retained. Type 2b intestinal metaplasia closer association with intestinal type gastric mucosa than other type.

Non specific chronic gastritis is very common disease. Its prevalence in US is not known, and increase incidence with age, mild form of chronic gastritis is asymptomatic.

Endoscopically and grossly, well develops atrophic gastritis and gastric atrophy produce thin, smooth mucosa with undue prominence of sub mucosal vessels. Three is an excellent correlations between gastric atrophy as estimated by endoscopic biopsy and result of acid. Conversely, the correlation of histology with symptomatology, radiology, and gasteroscopy is poor.

Chronic gastritis has been divided in to type’s having similar histologic feature (as already described) but a presumed different pathogenesis. The first type which is less common is designated as type A or immune. It usually affect the fundus in a diffuse manner, spares the antrum, and associated with antibodies to parietal cells, hypochlorhydria or achlorhydria, high serum of gatsterin levels. The alpha and beta subunit of gastric proton pump have been identified as major molecular target of this presumed auto-immune disease, which may evolve into pernicious anemia.
The other type, by far the most frequent, begins in the antrum and progresses proximally so that the fundic-pyloric border rises up gradually. This is referred to as type B or non-immune gastritis. In some classification schemes, this has been further subdivided into a form restricted to antrum and associated with hypochlorhydria and often duodenal peptic ulceration antrum and fundus in an initially patchy and eventually diffuse distribution (environmental gastritis).

Chronic atrophic gastritis usually presents as case of gastric carcinoma, and in general its severity is proportional to the extent of the tumor. Most case of gastric peptic ulcer is associated with antral and fundus gastritis, if present at all, is restricted to antrum. The incidence and extent of intestinal metaplasia are greatest in stomachs removed for carcinoma, least in those with duodenal ulcer, and intermediate in case of gastric ulcer.

The pathogenesis of type B gastritis is complex and properly multifactorials. Factors known to be statistically associated with this disorder include alcohol, tobacco, duodenal reflux, allergy to food, and various drugs, particularly anti-inflammatory agent.

The most important advance in field of chronic gastritis and other gastric disease (peptic ulcer, carcinoma, malignant lymphoma) has been awareness of the H.pylori. This organism, formerly known as campylobacter pylori, is a curved spirochete-like bacterium, which two
major genotypes exist. This organism colonizes gastric mucosa particularly the antrum and cardia in variety way; free in mucous, surface adhesion, and the intercellular colonization show greatest degree of epithelial damage. These changes include disintegration and loss of apical mucous with formation of epithelial pits and less frequently erosions and ulceration. The presumed main mechanisms for this alteration are motility and urease activity by organism. There also a relations between *H. pylori* and prevalence of lymphoid follicles.

*H. pylori* can be recognized in routine hematoxylin-easion stain and most intense that is all is need. However density of organism is low, its detection can be greatly facilitated by performance of special stains, which include Giemsa, Warthin-starry or Steiner sliver stains. With these techniques *H. pylori* has been found in 90% with chronic gastric and 95% of duodenal ulcer disease, 70% with gastric ulcer, and 50% with gastric carcinoma.

In 1991, a system was been proposed for comprehensives microscopic reporting gastritis. This method, referred to as “Sydney system” and upgrade in 1994, recommends the follow:

1 For natural and corpus biopsies to be assessed separately.

2 For gastric to be classified
Acute.

Chronic.

Special (e.g; lymphocytic, garnulomatous)

3 For the following variable to be graded

- H.pylori.
- Chronic inflammation.
- Neutrophils
- Intestinal metaplasia.

4 A concluding summary is to be provided, indicating the etiology (if known) topography (antrum, corpus, and pan-gastritis) and morphology include all variables.

1.4.2. Other type of gastritis:

1-Acute gastritis: May result of the ingestion of alcohol. Salicylates, and other form and other anti-inflammatory drugs, or by reflux of bile salt. Endoscopic biopsies, rarely taken in this condition, may show hyperemia, focal fresh hemorrhage, focal necrosis of surface and foveolar and neutrophils infiltration of the foveolar and glandular Lumina.

2- Hemorrhagic gastritis.

3- Collagenous gastritis.
4-Lymphcystic gastritis.

5-Allergic gastritis.

6-Diffuse esionophilic gastroenteritis.

7-Granulomatous gastritis.

1.4.3. Peptic ulcer and other benign ulcers:

Peptic ulcer: can occur wherever mucosa is bathed by gastric secretion. This includes the stomach, duodenum, lower third of esophagus, margins of a gasterojunostomy, and meckels' diverticulum with ectopic gastric mucosa. Acid peptic digestion is the ultimate cause for ulceration, but the mechanism that render the mucosa susceptible to this digestion are just as important for pathogenesis.

Duodenal ulcer (which are more comment than gastric ulcer, although their relative incidence seem to be decreasing) are classically associated with acid hyper-secretion, but most patient with gastric ulcer secrete either low normal or below normal amount of acid. Thus it would seem that the initial event in gastric ulcer is mucosal injury may be mediated in some instance by reflux of bile acid and pancreatic juices and is manifested anatomically by presence of gastritis ,an almost invariable finding in patient with peptic ulcer disease. In recent years, considerable evidence has accumulated suggesting that H.pylori plays crucial roles in
the pathogenesis of this disease. The risk of development of peptic ulcer is approximately 10 fold higher in patient with non atrophic H.pylori positive gastritis than in those with normal stomach, and the risk is increased further (twofold to threefold) when there is antral atrophy. Instead, the presence of corpus atrophy decease the incidence of ulcer (to practically zero levels when the atrophy is complete.

1.4.4. Acute peptic ulcer:

Is common finding at autopsy and usually a terminal event. It may also seen during life in any depleting illness, in sepsis, following surgery or trauma (stress ulcer), in patient with central nervous system injury or disease (Cushing ulcer) as complication of steroid treatment (steroid ulcer), in association with ingestion of aspirin, in patient with severe burns (curling ulcer), as complication of irradiation therapy or hepatic arterial chemotherapy, and following the introduction of tube in to the stomach. Marked epithelial atypical may be present in the gastric lesion resulting from hepatic arterial infusion chemotherapy. If ulcer involves only mucosa the process is designated as erosion. It can heal completely; however, if part is replaced by fibrotic tissue, leaving a depressed pit. Any of these ulcers, if deep enough, may perforate; this complication is particularly common in ulcer radiation therapy.

1.4.5. Chronic gastric ulcer:
Always occur in an achlorhydric zone of mucosa (an area of stomach lined by pyloric type of mucosa). Up to 90% of the ulcer are located on the lesser curvature (so called Magentrasse) near the incisaris angularis; however, since chronic gastritis is accompanied by antral metaplasia of fundal mucosa that advance proximally form the pylorus, peptic ulcer can be found anywhere in the stomach, although it is always surrounded by antral–mucosa.

The average age of the time of diagnosis is 50 years, but the disease can occur in any age group, including children. A male predilection exists but seems to be decreasing. Approximately 5% of ulcer is multiples. The radiographic diagnosis is approximately 95% accurate, but atypical cases can be distinguished with certainty carcinoma. Although some controversy persist, most author believe that ulcer of giant cells size over 3 cm, or those located in the greater curvature, do not indicate a height like hood of malignancy as formerly believed. The diagnosis of peptic ulcer has been greatly facilitated by use fiberoptic gasteroscopy, which allow the endoscopist to have a direct view of ulcer to photograph it, and obtain biopsies form edge; multiple biopsies about 10 or more are recommended for stander size ulcer.

Grossly, an active lesion is sharply delineated, usually oval or round but some time linear, with converging mucosal margin. The proximal folds
extending to it margin. The proximal margin tends to have overhanging edges, where the distal margin usually slope borders. On sections, there is undermining of the edge (especially on the proximal side) and complete replacement of muscular wall by grayish white fibrous tissue. On the serosal side, there may be sub-serosal fibrosis and inflammatory enlargement of regional lymph nodes. Prominent marginal nodulaty about the ulcer should suggest the presence of carcinoma; however, it should be remembered that it may be imposable to distinguish grossly a peptic ulcer from ulcerated carcinoma. As matter of fact, approximately 10% to 15% of gastric carcinoma appear as benign gastric ulcer.

Macroscopically, an active, well-developed, chronic peptic ulcer will show four more or less distinct layers (1) a surface coat of purulent exudates, bacteria, and necrotic debris; (2) fibrous necrosis; (3) fibrosis replacing muscle wall and extending into the sub-serosal. At the edges, the muscularis mucosa is seen fuse with the muscularis externa. Other common feature in the ulcer bed include thickening of vessels caused by sub-endothelial fibrous proliferation and hypertrophy of nerve bundle; both of these change are properly secondary events. The necrotic surface may superimposes infections by Candida albican.

As already stated, the mucosa surrounded, the ulcer is of pyloric type, including a component of gastrin (and somatostain) immunreactive cells
In case of infected with H. pylori, a typical constellation of morphologic change loss of the apical poratin and dropout of epithelial cells, epithelial pits, erosion, and cellular tufts, is seen in the ulcer edge.

Peptic ulcers can be classified according to their shape and size (round-oval, giant, linear) activity (open ulcer or ulcer scar), depth of penetration (sub-mucosa, muscularis externa, or beyond), or combination of criteria.

In the healing process of peptic ulcer regenerating epithelium grow over the surface. Any epithelium growing above an area where the muscularis mucosae are interrupted is regarded as regenerating. This epithelium often exhibits features of intestinal metaplasia and may contain chief and partial cells when the ulcer is located in the fundic areas, the presence of irregularities in the deep portion should not be misinterpreted as carcinoma. The danger of over diagnosis is particularly great in the ulcer cause by arterial infusion chemotherapy because of marked epithelial atypia that may be present.

**1.4.6. Treatment:**

The medical treatment of gastric ulcer consists of antacids and or H2-blockers. The usual criterion for adequate healing is reductions in the carter size of at least 50% over a 6 to 8 week period of intensive medical management. Failure to pass this test, development of complication
(hemorrhage, perforation, obstruction), and recurrence of ulcer is indicate for surgery. Giant ulcers size over (3 cm) is another quoted indication, although medical therapy should be successful in these cases. It should be remember that as many as 15% of gastric carcinoma may be pass healing test and some benign ulcer may actually enlarge during the test. The surgical procedures in general use for peptic ulcer are subtotal gasterentrostomy or pyloroplasty and vagotomy plus antrectomy. When a portion of stomach is removed, continuity is reestablished through a gasterojejunostomy (Billroth1) or gasterojunostomy (Billroth2). The long term results of surgery are good to excellent in over 80% of the patient.
1.5. OBJECTIVES

General objective:

To study gastric biopsy cases in KTH gastroendoscopic unit between 2008-2010, to determine the different clinic-pathological feature of these lesions.

Specific objective:

1. To determine the histological type of different gastric biopsy lesion.

2. To determine the anatomical location of different gastric lesion.
2-METHODOLOGY

2.1. Study design:

The study is descriptive retrospective recorded data-based study.

2.2. Study area:

The study was conducted at KTH, department of histopathology; it is one of major hospital in Sudan, providing nationwide diagnostic management, training and research services.

2.3. Study population:

Cases attended endoscopic department in KTH between January 2008- January 2010.

2.4. Inclusion criteria:

Case of gastric biopsy with full records and histological slides or paraffin wax embedded blocks.

2.5. Exclusion criteria:

Case with deficient record (missed request form) or missed histopathology slides and paraffin wax embedded blocks.
2.6. Data collection:

Data were collected from patients request form of histopathological department in KTH. The slides were collected and reviewed by investigator & supervisor to confirm the diagnosis of gastric lesion, determine the histological type. The slides were done from tissue fixed in 10% formalin for 24 hours or more. handled according to histological protocol, embedded in paraffin wax, sectioned by microtome of 3-5mm thickness of sections, and stained by hematoxylin and eosin stain, some case of suspect clinically diagnosis of H pylori gastritis are stain rotainly by Gemsa and silver stain to detected H.pylori microorganism.

2.7. Data analysis:

The data were analyzed statistically using computer using Statistically Package For Social (SPSS). Chi square test was calculated to compare the association.
3. RESULTS

This study is conducted in hundred patient admitted in KTH in endoscopic unit of gastroenterology last two years.

3.1-Characteristics of studied population:

3.1.1 Sex distributions:

Fifty one patient (51%) form studied patient are male, and forty seven (47%) patients are female. The female to male ratio are 1:1

3.1.2-Presence of upper gastrointestinal symptom among studied population.

The various clinical symptom of different gastric lesion are ninety eight (98%) of case were complain of upper GIT symptom, and only tow (2%) of case has no symptom.

3-Distribuation of benign verus malignant lesion among the studied population:

About eighty one 81% of patient are diagnosis as benign gastric biopsy and nineteen 19% are diagnosis as malignant gastric biopsy.
3.1.4 Anatomical location of endoscopic biopsy.

The most common site of endoscopic biopsies areas are seventy (70%) of case form antrum and twenty three (23%) of case form the fundus, and eighteen (18%) of case form the body, and seven (7%) of case form unknown site.

3.1.5-Type of endoscopic finding:

The most common type of endoscopic finding are seventy (70%) of case are show ulcerated mucosal surface, thirty one (31%) of case show normal mucosal surface, and eighteen (18%) are show gastric mass.

3.1.6- Common histological finding:

Most common histological type of gastric biopsy among studied population are fifty tow( 51%) of case are gastritis , the second are ninety one(19%) of case are diagnosis as gastric adenocarcionma third are sixteen (16%) are gastric polyps, the last are four( 4%) are diagnosis as normal gastric biopsy.

3.1.7- Type of gastritis:

Most case is H.pylori associated gastritis are about fifty-seven (57%) of case and non specific gastritis are about forty two (42%).
3.1.8-Histological grading among H.pylori type of gastritis:

Severe gastritis are about 50 % of case, severe active are thirty six (36 %) mild form are ten(10%), of case and moderate form are four(4%) of cases.

3.1.9- Type of peptic ulcer:

About sixty eight (68%) of cases are acute peptic ulcer and thirty one (31%) of cases are chronic peptic ulcer.

3.1.10-Relation between histological type and endoscopic site of biopsy:

a) The total number of gastritis are about 52 of case and about twenty five(25 ) of case of show ulcerated mucosal surface , while twenty three( 23) of case show no endoscopic finding and only four (4) case show endoscopic mass.

b) About sixteen of case diagnosis as peptic ulcer disease and fifteen (15) of peptic ulcer are show ulcerate mucosal surface, while only one case (1) are show normal gastric mucosa.

c) About nineteen of cases are diagnosis as adenocarcinoma and thirteen (13) of them are show gastric mass, while three( 3) of case are show ulcerated mucosal surface.
d) Only four (4) case of gastric biopsy are show normal endoscopic finding.

3.1.11- Relation between age group and type of gastritis.

a) Most common age group are young adult (20-40) are 14 cases of H pylori and 12 of the case are non specific type of gastritis.
b) Adult age group (40-60) years are 9 of the case of H.pylori associated gastritis and 7 case of non specific gastritis
c) Old age group (60-80) year's are2 of case are H.pylori associated and 8 of cases are non specific gastritis.

3.1.12- Relationship between age group and histologic garde of the non specific gastritis:

a) Ten(10) of case of non specific gastritis with age group young adult (20-40) years has severe form histological type gastritis while 2 of case show mild form.
b) Six (6) of case of non specific gastritis with in age group (40-60) showing severe form of histological and only one case show mild form.
c) Two( 2) of case non specific gastritis with elderly age group( 60-80) severe form of histological gastritis and only one case is show mild form.
4. DISCUSSIONS

This study is a retrospective cross-sectional one addressed to review of clinic-pathology of gastric biopsy in endoscopic unit of KTH between January 2008-January 2010 and include analysis of 100 case of 51% of male and 49% is female.

One aim of this study is to detect the most common gastric lesion type that diagnosed by gastric biopsy, so that the most common gastric lesion is 80% benign versus 19% malignant and most common benign lesion that is gastritis, peptic ulcer and gastric polyps. Also we detected that the most age group among the benign gastric lesions are 20-60 years, where the most age group among malignant lesion properly adenocarcinoma are age 60-80 years. These results are agreements with previous studies. (see literature review)

In our present study that conducted among 52 case of gastritis the prevalence age distribution between the 20-60 years, and still present in older age more than 60 years, these similar with study done by Dr Sipponen, Department of pathology-Jovy hospital in Finland.

Endoscopic immersion as well as so information thought other image modalititis is likewise extremely important, in our study we found that the most common finding is ulcerated mucosa, erosion, and mass
these and 51% of case of gastritis are present with gastric mucosal abnormality seen by endoscopic camera, few case about 13 % are present with normal endoscopic finding ,also association between chronic gastritis and peptic ulcer disease and mucosal abnormality ,these are agreement with previous studies.

This study is indicate that the most site of gastric biopsy is antral and fundus, pyloric area and these are most common site for colonization of H.pylori and most common site for gastric carcinomas, several study was carried out and show similarity such as study support by the institute of anatomic pathology., histology of internal medicine –gastroenterology department of University of Prihtina, and Dr-Sipponen, Department of histopathology of Jovy hospital in Finland.

Most laboratories use H&E stain for routine evaluation of gastric biopsy our study are indicate that in52 of case of gastritis are 30 of case are positive by H&E stain confirm by special stain e.g: Gemsa stain, yield 57% ,these result is very close to comparing study that done in Alexandria University by Dr .Hodia.

This study indicate that most case with H.pylori associated gastritis has phenotypic appearance of severe form of gastritis, few case are present with moderate form of gastritis, this grade of gastritis are depend on mainly H&E stain , and some special stain, so lack of definitive
information that need to application of Sydney classification for gardening of gastritis such as of etiological finding, topographical, adequacy of sampling with proper labeling so we depend only on the histological finding for grading of gastritis.

Most histological type of gastric adenocarcinoma is intestinal type, and most common site is in pyloric area. These are compatible with literature review.
4.1. CONCLUSION

Regardless of limitation of this study, it's indicated that our country shares many clinical and pathological characteristics with other countries.

These characteristics are include most common benign gastric lesion are gastritis, gastric polyps and peptic ulcer lesion. And most common malignant lesion is gastric adenocarcinoma.

The age distributions of benign gastric lesion are young age group, while age distributions of malignant lesion are old age group.

Most anatomical site of benign gastric lesion are located in antral and fundus region of stomach and associated with mucosal abnormalities proofed by endoscopic view and histological sections. Major cause of gastritis is H.pylori and associated with severe form of gastritis. Most malignant lesion are adenocarcinoma are located in pyloric areas and endoscopic finding are projecting mass or ulcer.
4.2. RECOMMENDATIONS

Further in-depth, prospective study is highly recommended to carry out in more than one center for more evaluation.

- Good communication between the pathologist and gastroenterologist are needed for further improvement of gastric biopsy result in correlation with other non-invasive tests for detection of H.pylori microorganisms.
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