

CHAPTER II

LITERATURE REVIEW

A. The Concept of Dyspepsia Syndrome

1. Definition of Dyspepsia Syndrome

Dyspepsia syndrome is a collection of symptoms originating from the gastroduodenal region, characterized by complaints such as early satiation, postprandial fullness, epigastric pain, and epigastric burning (Wauters et al., 2021). Based on the Rome IV criteria, these four complaints are the cardinal symptoms of dyspepsia that can occur individually or simultaneously, and are often accompanied by other symptoms such as upper abdominal bloating, nausea, and belching. A diagnosis of dyspepsia syndrome is established if the symptoms have persisted for at least the last three months, and an individual is considered positive if they experience at least one of these four cardinal symptoms (Rome Foundation, 2019).

2. Etiology of Dyspepsia Syndrome

The etiology of dyspepsia syndrome is highly variable and can be categorized into organic (structural) causes, infections, medication effects, and functional disorders involving gut-brain interactions.

a. Mucosal Structural Abnormalities

The most common organic cause found in patients presenting with dyspeptic complaints is damage to the integrity of the gastric and duodenal lining. These conditions include peptic ulcers (gastric/duodenal ulcers), erosive gastroduodenitis (inflammation with erosion), and gastropathy. This mucosal damage causes direct exposure of the gastric nerves to acid, which triggers epigastric pain.

b. Helicobacter pylori Infection

The presence of *H. pylori* bacteria is a significant etiological factor in the pathogenesis of dyspepsia. *H. pylori* infection has been proven to have a significant relationship with the onset of abdominal pain and indigestion.

This bacterium causes chronic inflammation of the gastric mucosa, which contributes to the emergence of clinical complaints.

c. Medication Effects

The chronic use of certain medications can irritate the gastric mucosa and trigger dyspeptic symptoms. The use of non-steroidal anti-inflammatory drugs (NSAIDs) and certain antibiotics (such as doxycycline) acts as a trigger for esophagitis and erosive gastritis. These medications work by disrupting the mucosal defense barrier or aggressively increasing gastric acidity (Cappell, 2023).

d. Gut-Brain Axis Interaction

In cases of functional dyspepsia (without organic abnormalities), the primary etiology is a disruption in communication between the central nervous system and the digestive system. Functional gastrointestinal disorders have a bidirectional relationship with psychological disturbances. Stress, anxiety, and mood disturbances can trigger visceral hypersensitivity. This condition can cause normal signals from the stomach to be exaggeratedly perceived as pain by the brain.

e. Gut Dysbiosis

Alterations in the composition of intestinal bacteria, or dysbiosis, have also been identified as a causative factor. An imbalance in normal gut flora can trigger a low-grade inflammatory response and motility disorders. This condition frequently underlies symptoms of persistent bloating, fullness, and postprandial discomfort in dyspeptic patients (Rizvi et al., 2023).

3. Clinical Manifestations of Dyspepsia Syndrome

According to the United European Gastroenterology and European Society of Neurogastroenterology and Motility Consensus (2021), the hallmark symptoms that serve as primary indicators in dyspepsia patients are known as "cardinal symptoms," which include postprandial fullness, early satiation, epigastric pain, and epigastric burning.

a. Postprandial Fullness

Postprandial fullness is the most frequently reported symptom. This condition is described as an uncomfortable sensation akin to food being retained in the stomach for an extended period, even when the consumed portion is normal. A gastric motility disorder mechanism prevents food from being promptly propelled into the intestines, resulting in prolonged gastric distension.

b. Early Satiation

Early satiation is the inability to finish a normal-sized meal. This symptom appears shortly after the patient begins eating, where the stomach feels full even though the meal is not yet finished. This condition is often associated with impaired gastric fundus accommodation, which fails to relax upon receiving food intake, thereby drastically reducing functional gastric capacity.

c. Epigastric Pain

Epigastric pain is an intense, subjective sensation of pain in the epigastric region. Unlike ordinary discomfort, this pain is perceived as sharper and more disruptive to activities. Patients typically report that the pain is not always related to food intake; it can occur on an empty stomach or after meals, which is associated with visceral nerve hypersensitivity to stimuli.

d. Epigastric Burning Epigastric burning is an uncomfortable, hot sensation in the epigastric area. This symptom is specifically felt in the epigastrium and does not radiate to the chest (distinguishing it from heartburn in GERD). This sensation is often triggered by mucosal irritation or hypersensitivity to gastric acid.

e. Accessory Symptoms

These include symptoms such as upper abdominal bloating, persistent nausea, and excessive belching (United European Gastroenterology, 2021).

4. Complications of Dyspepsia Syndrome

According to recent reviews in the *Frontiers in Medicine* journal (2025) and the British Society of Gastroenterology guidelines on the management of functional dyspepsia (2022), chronic dyspepsia can lead to various complications that affect the physical and psychological well-being, as well as the quality of life of sufferers.

a. Physical and Nutritional Complications

1) Unintentional Weight Loss

Weight loss is a tangible physical complication in chronic dyspepsia patients. This condition occurs due to the early satiation mechanism and a fear of eating following postprandial pain, which forces patients to drastically restrict their caloric intake below the body's daily requirements. If left untreated, this can culminate in nutritional deficiencies.

2) Overlap Syndrome

Dyspepsia patients are at a high risk of developing overlapping complications with other gastrointestinal disorders. Studies indicate that up to 37% of dyspepsia patients also develop Irritable Bowel Syndrome (IBS) and Gastroesophageal Reflux Disease (GERD). The presence of these comorbidities worsens the prognosis and complicates treatment as the symptoms become more complex (e.g., epigastric pain accompanied by bowel habit changes or a burning sensation in the chest).

b. Psychosocial Complications and Quality of Life

1) Sleep Disturbances

Sleep disturbance is an often-overlooked yet highly disruptive complication. Persistent abdominal discomfort, especially at night, leads to high rates of insomnia and poor sleep quality in dyspepsia patients. This has a direct impact on chronic daytime fatigue.

2) Psychological Comorbidities

Dyspepsia has a strong bidirectional relationship with mental health. Recurrent and chronic symptoms have been proven to trigger anxiety and depression in the majority of patients. The psychological stress arising from this illness subsequently creates a vicious cycle, wherein the stress exacerbates gastric pain sensations via the gut-brain axis.

5. Diagnosis of Dyspepsia Syndrome

The diagnosis of dyspepsia is established based on clinical complaints and diagnostic tests to differentiate between functional dyspepsia and organic dyspepsia.

a. Symptom-Based Questionnaire

Initial diagnosis, particularly in research contexts or primary care, frequently utilizes standardized questionnaires based on the Rome IV criteria, which serve as the international reference for diagnosing functional dyspepsia. These criteria identify patients based on the presence of four cardinal symptoms: bothersome postprandial fullness, bothersome early satiation, bothersome epigastric pain, and bothersome epigastric burning. Based on these symptoms, dyspepsia is classified into two main clinical subtypes: Postprandial Distress Syndrome (PDS), characterized by meal-related complaints such as fullness or early satiation occurring at least three days a week; and Epigastric Pain Syndrome (EPS), characterized by pain or burning in the epigastrium occurring at least one day a week. In rigorous medical diagnosis, the Rome IV Criteria stipulate that these symptoms must have been present for the last three months, with symptom onset at least six months prior to diagnosis (Rome Foundation, 2019). However, for preliminary screening purposes without further examination, an individual is categorized as experiencing dyspepsia syndrome if a collection of active symptoms has been felt within the last three months, provided that if they indicate or answer 'yes' to even one of the four main symptom questions (bothersome fullness, early satiation,

epigastric pain, or epigastric burning), they can already be classified as having dyspepsia syndrome (Amanda et al., 2025).

b. Upper Gastrointestinal Endoscopy (Gastroscopy)

Endoscopy is recommended as the gold standard for diagnosis, particularly for patients over the age of 55 or those exhibiting "alarm features" such as weight loss, dysphagia, or persistent vomiting. This examination aims to rule out the possibility of gastric cancer, peptic ulcers, or esophagitis. If the endoscopy results are normal, the patient is diagnosed with functional dyspepsia.

c. Helicobacter pylori Testing In patients without alarm features, a "test and treat" strategy is highly recommended. Patients are tested for the presence of H. pylori bacteria through a urea breath test or a stool antigen test. If positive, the diagnosis points toward H. pylori-associated dyspepsia (Wauters et al., 2021).

6. Management of Dyspepsia Syndrome

According to Syam (2023) in *The 2022 Indonesian Consensus Report*, the management of dyspepsia is divided into two main approaches: pharmacological and non-pharmacological management, as follows:

a. Pharmacological Management

- 1) Empirical Acid-Suppressive Therapy (Proton Pump Inhibitor/PPI) The administration of PPIs (such as omeprazole, lansoprazole, or esomeprazole) is recommended as first-line therapy in dyspepsia patients without alarm features. Syam (2023) states that PPIs work effectively to suppress gastric acid production to relieve epigastric pain and burning sensations, with a strong recommendation level.
- 2) Combination with Prokinetics If the response to a single PPI is inadequate, the addition of prokinetic drugs (such as domperidone or metoclopramide) may be considered. Prokinetics function to accelerate gastric emptying, which is highly beneficial for patients with predominant complaints of fullness and early satiation.

3) *Helicobacter pylori* Eradication Therapy For patients confirmed positive for *H. pylori* infection via diagnostic tests, combination antibiotic therapy (such as amoxicillin, clarithromycin, and a PPI) must be administered for 14 days. This "test and treat" strategy is deemed effective in preventing long-term recurrence and peptic ulcer complications

b. Non Pharmacological Management

- 1) *Dietary and Nutritional Modification* Dietary regulation is highly emphasized to reduce the frequency of recurrence; patients are advised to avoid foods that are irritating or that delay gastric emptying, such as spicy, acidic, and high-fat foods, as well as carbonated and caffeinated beverages. Eating small, frequent meals is also recommended to reduce the stomach's workload.
- 2) *Lifestyle and Physical Activity Modification* The Rome Consensus advises patients to engage in regular aerobic physical activity, quit smoking, and avoid alcohol. Regular physical activity has been shown to improve gastrointestinal motility and reduce symptom severity in dyspepsia patients.
- 3) *Stress and Psychological Management* Given the close relationship between the brain and the gut (gut-brain axis), stress management is an essential component. For patients with refractory symptoms or those triggered by anxiety, psychotherapy or counseling approaches can be provided to break the stress cycle that exacerbates physical symptoms.

B. Factors Associated with Dyspepsia Syndrome

1. Stress Level

Stress is a non-specific bodily reaction to any demand or burden that disrupts it, originating from either internal or external factors. Generally, stress levels can be classified into several categories ranging from mild, moderate, to severe, which can be measured using the DASS-42 questionnaire (Putra et al., 2025).

Stress is a key factor in the pathophysiology of functional dyspepsia, hence this condition is classified under Disorders of Gut Brain Interaction (DGBI). Through the Gut-Brain Axis mechanism, psychological stress is processed in the cerebral cortex and transmitted to the hypothalamus, which subsequently activates the Hypothalamic-Pituitary-Adrenal (HPA) axis and the sympathetic nervous system simultaneously. Activation of the HPA axis increases the secretion of the hormone cortisol, which decreases gastric mucosal protection and increases gastric acid production. Concurrently, activation of the sympathetic nervous system leads to decreased contractility and impaired gastric motility, including delayed gastric emptying. This combination of increased gastric acid and motility disturbances plays a role in the onset of functional dyspepsia symptoms, particularly in individuals with high stress levels such as academic stress, thereby reinforcing the link between psychological stress and the occurrence of DGBI (Putra et al., 2025).

Putra (2025) found a highly significant relationship ($p = 0.001$) between academic stress and the incidence of functional dyspepsia in first-year university students. The more severe the stress level (due to new environmental pressures), the higher the risk of experiencing DGBI disorders. Meanwhile, Suhesti (2025) found a significant relationship ($p = 0.041$) among adolescents in an orphanage, where psychological pressure triggered neurogenic pathways that stimulated excessive gastric acid secretion.

To measure stress levels, this study utilizes a standardized instrument, namely the DASS-42 (Depression Anxiety Stress Scales) questionnaire, which is designed to assess the respondents' emotional and physical responses to experienced pressures. Although Lovibond & Lovibond (1995) divided stress levels into five categories, for the purpose of analyzing its relationship with functional dyspepsia in this study, the categorization is simplified into two main groups: the good/non-risk category (encompassing normal and mild stress) and the at-risk category (encompassing moderate to extremely severe stress). The details of this grouping can be seen in the following table:

Table 2.1 Classification of Stress Levels

Score <i>DASS-42</i>	Classification	Research categories
0-14	Normal	Risk-Free (Good)
15-18	Lightweight	
19-25	Medium	Risky (Bad)
26-33	Severe	
>33	Very Heavy	

2. Dietary Pattern

Dietary pattern is defined as daily consumption behavior that encompasses the frequency, schedule, and types of food consumed. A healthy dietary pattern to prevent dyspepsia is characterized by eating regularly, avoiding large meals at one time, and avoiding specific trigger foods (National Institute for Health and Care Excellence, 2019).

In the pathophysiology of dyspepsia syndrome, dietary patterns play a central role due to their direct influence on the physiological mechanisms of the stomach. This relationship is explained through two main mechanisms. First, the mechanism of delayed gastric emptying, where consuming excessively large portions or high-fat foods slows down the stomach's emptying process. This condition increases gastric distension or stretching of the stomach wall, which subsequently triggers symptoms of fullness and bloating (BSG, 2022). Second, the mechanism of gastric acid secretion dysregulation caused by irregular eating schedules and the habit of rapid eating. This behavior disrupts the circadian rhythm of gastric acid secretion, resulting in excessive acid exposure to an empty gastric mucosa, thereby causing epigastric pain and burning sensations (Kefi et al., 2022).

Various empirical evidence has confirmed the close relationship between dietary patterns and dyspepsia. Putra et al. (2025), in their study on first-year students at Universitas Muhammadiyah Mataram, found a significant relationship ($p = 0.001$) between dietary regularity and the incidence of functional dyspepsia, where students with irregular eating habits had a much higher risk of experiencing symptoms. These findings are supported by a

Systematic Review by the BSG (2022), which reported that dietary factors are symptom triggers complained about by approximately 80% of functional dyspepsia patients. Furthermore, NICE guidelines (2019) specifically highlight that the habit of skipping breakfast or eating late at night is closely associated with an increased frequency of symptom recurrence, especially in the young adult population.

To measure this variable, the study uses the Dietary Habits Questionnaire instrument, which adopts indicators of the regularity of main meal schedules (breakfast, lunch, dinner) and meal frequency. The assessment is grouped into two categories: the 'Regular' (good) category if the respondent eats main meals routinely every day and rarely skips mealtimes, and the 'Irregular' (poor) category if the respondent frequently skips one of the main meals or has an erratic, changing eating schedule (Amanda et al., 2025).

3. Consumption of Irritating Foods

Irritating foods are foods or beverages that can trigger dyspepsia symptoms. This triggering mechanism occurs through two main pathways: by stimulating excessive gastric acid production or by directly irritating the gastroduodenal mucosal lining (Zakiyah et al., 2021). Different types of food have specific mechanisms in affecting the stomach. Spicy foods, for instance, contain capsaicin, which can irritate the gastric mucosa and increase the sensation of burning pain (heartburn), whereas acidic foods like vinegar and citrus fruits can lower gastric pH, exacerbating irritation. On the other hand, high-fat foods affect motility by delaying gastric emptying time, thereby causing feelings of fullness and bloating. In addition to food, caffeinated beverages (coffee, tea) and carbonated beverages (soda) are also known to stimulate excessive gastric acid secretion and trigger the relaxation of the lower esophageal sphincter, which causes reflux (Suhesti & Amanda, 2025).

The clinical impact of these consumption patterns is supported by empirical evidence from research by Suhesti and Amanda (2025). The study, conducted on adolescent populations and primary healthcare center (Puskesmas) patients, found a highly significant relationship ($p < 0.001$)

between the habit of consuming irritating foods or beverages and the incidence of dyspepsia, where excessive consumption serves as a strong predictor of symptom onset.

To measure this variable, the study utilizes a Food Frequency Questionnaire (FFQ) instrument specifically designed to record how often respondents consume specific types of foods such as spicy, acidic, coconut milk-based, and caffeinated foods/beverages. The assessment is grouped into two categories: the 'Regular' (Good) category if the respondent rarely or never consumes irritating foods/beverages (frequency < 3 times per week), and the 'Irregular' (Poor) category if the respondent frequently consumes irritating foods/beverages (frequency ≥ 3 times per week), which theoretically can trigger cumulative irritation of the gastric mucosa (Kefi B, et al., 2022).

4. Use of NSAIDs (Non-Steroidal Anti-Inflammatory Drugs)

NSAIDs (Non-Steroidal Anti-Inflammatory Drugs) are a class of medications commonly used by the public to relieve pain, reduce fever, and treat inflammation. Examples of frequently used drugs include ibuprofen, mefenamic acid, and aspirin (Sidik, 2024). However, the use of these drugs has a close relationship with the risk of gastric mucosal damage, which is explained through a pathophysiological mechanism of enzyme inhibition. NSAIDs work by inhibiting the cyclooxygenase (COX) enzyme, despite this enzyme playing a vital role in producing prostaglandins that serve to protect the gastric mucosal lining (cytoprotection). Due to this inhibition, prostaglandin production drops drastically, causing the stomach wall to lose its natural protection and become vulnerable to irritation by gastric acid. This condition can trigger erosions leading to ulcers, resulting in organic dyspepsia, and recent guidelines also mention that NSAIDs can trigger symptoms in functional dyspepsia (Black et al., 2022).

Empirical evidence regarding this relationship was demonstrated by Amanda, et al. (2025) in their study on factors associated with the incidence of dyspepsia. The study found a statistically significant relationship between the

use of Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) and the incidence of dyspepsia syndrome, where the proportion of gastric complaints was found to be higher in the group of respondents who had a history of consuming pain relievers compared to those who did not.

To assess this variable, the instrument used is the NSAID Use History Questionnaire. This is an instrument consisting of 3 question items to identify respondents' habits in consuming pain relievers (such as ibuprofen, aspirin, mefenamic acid, and piroxicam) in specific situations, namely during abdominal pain, headaches, or after delayed meals. Based on a dichotomous scoring system, the assessment is grouped into two categories: the 'Not At-Risk' category if the respondent has no history of use at all (Total Score = 0), and the 'At-Risk' category if the respondent has a history of using the medication (Total Score = 1), indicated by a 'Yes' answer to any of the question items (Amanda et al., 2025).

5. Sleep Quality

Sleep quality is an individual's satisfaction with their sleep experience, which encompasses aspects of sleep initiation (ease of falling asleep), sleep maintenance (duration and depth), and feeling refreshed upon waking. Poor sleep quality is typically characterized by symptoms of difficulty initiating sleep, frequent nighttime awakenings, or inadequate sleep duration. Clinically, sleep quality can be measured using the standardized Pittsburgh Sleep Quality Index (PSQI) instrument, which classifies a person's sleep status into two main categories: good sleep quality (PSQI score ≤ 5) and poor sleep quality (PSQI score > 5).

The relationship between sleep disorders and dyspepsia occurs through complex neuro immunological pathways that affect the digestive system. This mechanism involves the activation of the Gut-Brain Axis, where sleep deprivation is considered a physical stressor that disrupts the regulation of the gut-brain axis, thereby increasing sympathetic nervous system activity and cortisol hormone secretion, which triggers excessive gastric acid production.

Furthermore, poor sleep increases immune system activation and the release of pro inflammatory cytokines that can trigger or worsen gastric pain symptoms (Khairunisa & Nasution, 2024). Another mechanism involves the reduction of melatonin hormone levels due to irregular sleep. Melatonin possesses a gastro-protective effect by increasing mucosal blood flow and reducing acid secretion; thus, a decrease in this hormone makes the stomach more vulnerable to irritation.

Empirical evidence regarding this relationship was demonstrated by Khairunnisa and Nasution (2024) in their study on final-year students at the Faculty of Medicine, Universitas Muhammadiyah Sumatera Utara. The study found a significant relationship ($p = 0.01$) between sleep quality and the incidence of functional dyspepsia, where the proportion of dyspepsia occurrence was found to be much higher in the group of students who had poor sleep quality.

To assess this variable, the instrument used is the Pittsburgh Sleep Quality Index (PSQI) questionnaire. This is an international standard instrument (Gold Standard) consisting of 19 question items to assess 7 components of sleep (including subjective quality, latency, duration, efficiency, sleep disturbances, use of sleep medication, and daytime dysfunction) over the past month. Based on the standard PSQI scoring system, the assessment is grouped into two categories: the 'Good' category if the respondent has a healthy and refreshing sleep pattern (Total PSQI Score ≤ 5), and the 'At-Risk' category if the respondent experiences significant sleep disturbances (Total PSQI Score > 5) (Nurjanah et al., 2024).

C. Theoretical Framework

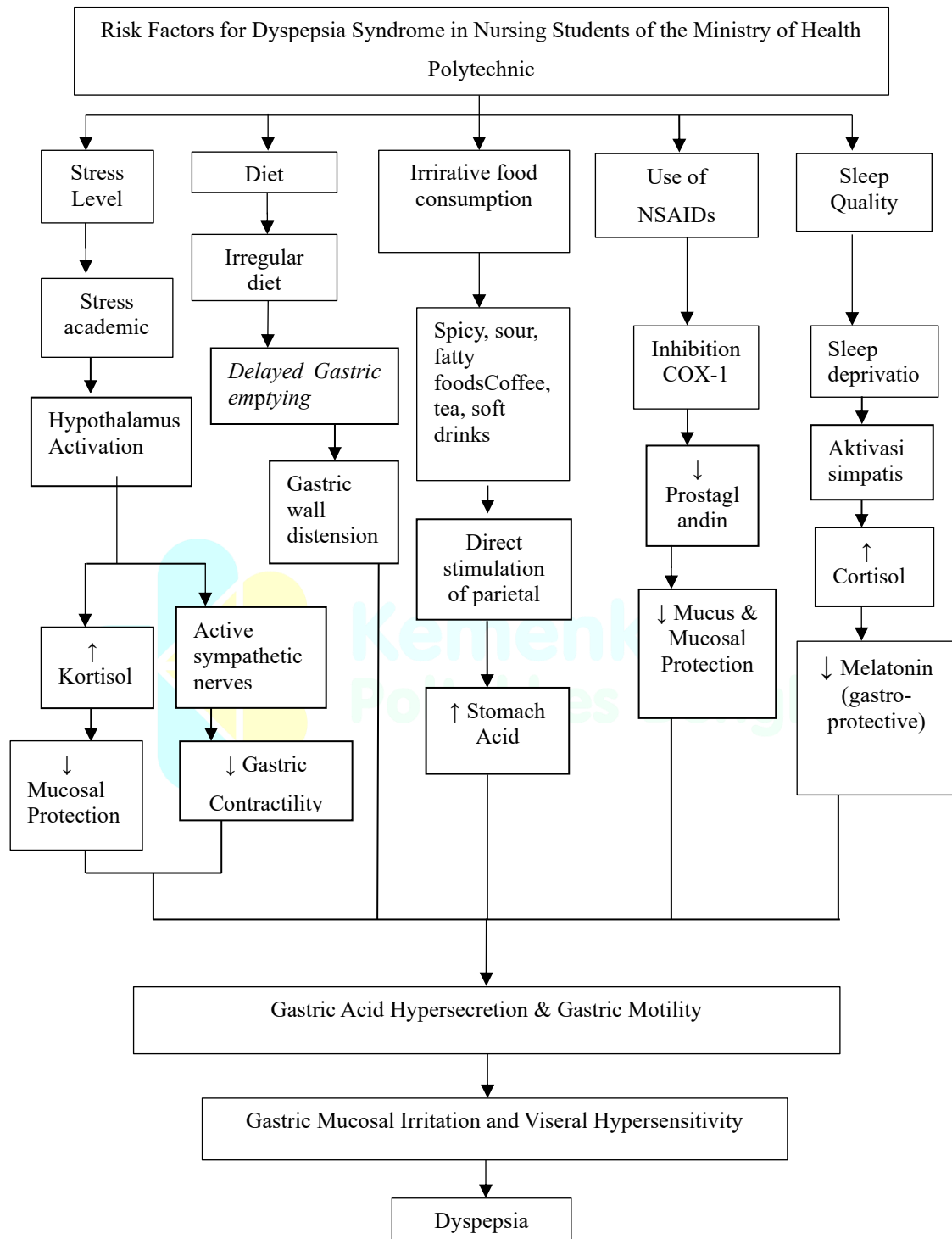


Table 3.1 Theoretical Framework

Sources: Syam *et al.*, (2023) and Khairunisa & Nasution (2024)