

Current concepts on Eating Disorders, Etiology and Treatment

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Abstract: Anorexia nervosa (AN), bulimia nervosa (BN) and obesity are eating disorders (ED) are considered to be mental illness, while other contends ED is symptoms of starvation. ED is prevalent worldwide increased prevalence in the west, and in the high income Southeastern countries, female predominance than male. Risk factors include genetic factors psychologic, personal characters, socioeconomic and western culture. Bacterial, parasitic infections play an important role. Eating behavior is controlled by neuroendocrine system, with Hypothalamus-pituitary-adrenal-axis (HPA axis) a major component. Physical symptoms of ED are weakness, fatigue, sensitivity to cold, reduced libido, and weight loss. Polycystic ovary syndrome (PCOS) is the common endocrine disorder to affect women. Medical history is important and all organic causes should be excluded prior to a diagnosis of a ED. Prognosis for AN and BN, recovery rates are up to 50% to 85% range. Ten per cent mortality in AN and BN, a Canadian study reported highest mortality than normal population. Effective psychotherapeutic treatments are still lacking due to complex treatment outcome variables. Prevention to aim a healthy development before the occurrence of ED, on-line program provides avenues for prevention.

Keywords: Eating disorders, Anorexia nervosa, Bulimia nervosa, Etiology.

I. Introduction:

Eating disorders (ED) are mental illness defined by abnormal eating habits that negatively affect a person's physical or mental health [1]. The cause of ED is not clear. Both genetic and environmental factors appear to play a role [2]. Cultural idealization of thinness is believed to contribute for example affect about 12 % of dancers [2,3]. Those who have experienced sexual abuse are also likely to develop ED [4]. Some disorders such as pica and rumination disorder occur more often in people with intellectual disabilities. Only one disorder can be diagnosed at a given time [1]. In the developed world ED affects about 1.6% of women and 0.8% of men in a given year. Anorexia affects about 0.4% and bulimia affects about 1.3% of young women in a given year [1]. Anorexia and bulimia occur nearly ten times more often in females than males [1]. ED result in about 7,000 deaths a year as of 2010, making them the mental illness with the highest mortality rate [5]. Total costs in USA for hospital stays involving DE rose from \$165 million in 1999-2000 to \$277 million in 2008-2009. The mean cost per discharge of DE rose from \$7,300 to \$9,400 [6]. Rates of ED appear to be lower in less developed countries [7]. Population based studies on the prevalence of ED, attitude and behaviors pertaining to the fear of fatness [8], among young females in high income East Asian societies such as Japan, Singapore, Hong Kong, Republic of Korea, and Taiwan found a similar behavior [9,-12]. The psychopathology of DE in Singapore is very similar to that in the western countries [10, rpt]. Prevalence of DE in India was 1.25% [13]. Physical symptoms of DE are weakness, fatigue, sensitivity to cold, reduced beard growth in men, reduction in waking erection, reduced libido, weight loss and failure of growth [14]. Treatment involves counselling, a proper diet, and reduction of efforts to eliminate food, hospitalization, and medication for associated symptoms [15]. The paper reviews the current literature, etiology, pathophysiology, clinical symptoms and treatment of eating disorders.

II. Etiology

Many people with DE suffer also from body dysmorphic disorder (BDD), altering the way a person sees himself or herself [16]. Studies have found that a high proportion of individuals diagnosed with BDD also had some type of eating disorder, with 15% of individuals having anorexia nervosa or bulimia nervosa [16]. The link between BDD and anorexia stems from the fact that both BDD and anorexia nervosa are characterized by preoccupation with physical appearance and a distortion of body image [17]. There also many other possibilities such as environmental, social, and interpersonal issues that could promote and sustain these illnesses [18]. Also the media are oftentimes blamed for the rise in the incidence of eating disorders due to the fact that media images of idealized slim physical shape of people such as model and celebrities motivate or even force people to attempt to achieve slimness themselves. While past findings have described the causes of eating disorders as

primarily psychological, environmental, and sociocultural, new studies have uncovered evidence that there is a prevalent genetic/heritable aspect of the causes of eating disorder [19].

Genetic factors: Numerous studies have shown a possible genetic predisposition toward ED as a result of Mendelian inheritance [20]. It has also been shown that ED can be heritable. Recent twin studies have found slight instances of genetic variance when considering the different criterion of both anorexia nervosa and bulimia nervosa as end phenotypes contributing to the disorders as whole [18]. In other recent study, twin and family studies led researchers to discover a genetic link on chromosome 1 that can be found in multiple family members of an individual with anorexia nervosa, indicating an inheritance pattern found between family members of others that have been previously diagnosed with an eating disorder [19]. A study found that an individual who is a first degree relative of someone who has suffered or currently suffers from an eating disorder is seven to twelve times more likely to suffer from an eating disorder themselves [21]. Twin studies also have shown that at least a portion of the vulnerability to develop eating disorders can be inherited, and there has been sufficient evidence to that there is a genetic locus that shows susceptibility for developing anorexia nervosa [21]. One of the limitations of twin study could be due to the short follow up period. Some of the cases that are not concordant may turn concordant later, and unaccounted cases can affect heritability estimate for eating disorders. Small sample size is another limitation in twin studies that prohibits researchers to study wide range of non-shared and shared environmental effects, and probably overestimates rate of heritability. The study of larger sample size that preferentially includes different racial groups would be more useful [2]. In 2015, the world's largest genetic investigation into anorexia nervosa was launched, the Anorexia Nervosa Genetic Initiative (ANGI), an international research study aiming to recruit over 13000 blood donations from the people with experience of the disorder in order to detect genetic variations that may contribute to this illness [22].

Epigenetic mechanisms are means by which environmental effects alter gene expression via methods such as DNA methylation; these are independent and do not alter the underlying DNA sequence. They are heritable, but also may occur throughout the lifespan, and are potentially reversible. Dysregulation of dopaminergic neurotransmission due to epigenetic mechanisms has been implicated in various eating disorders [23].

Psychologic factors. Eating disorders are classified as Axis 1 disorders in the Diagnostic and Statistical Manual of Mental Health Disorders (DSM-IV), published by the American Psychiatry Association (APA). There are various other psychological issues that may factor into eating disorders, some fulfill the criteria for separate Axis 1 diagnosis or a personality disorder which is coded Axis 11 and thus are considered comorbid to the diagnosed eating disorder. Axis 11 disorders are subtyped into "3 clusters" A, B, and C. The causality between personality disorders and eating disorders has yet to be established [24,25]. Some people have a previous disorder which may increase their vulnerability to developing an eating disorder. Some develop them afterwards [26,27]. The severity and type of eating disorder symptoms have been shown to affect comorbidity [28]. DSM-IV should not be used by the laypersons to diagnose themselves, even then used by professionals there has been considerable controversy over the diagnostic criteria used for various diagnoses, including eating disorders. There has been controversy over various editions of the DSM including latest edition DSM-V, May 2013 [29].

Personality characters. There are various childhood personality characters (traits) associated with the development of eating disorders [30]. Many personality characters have genetic component and are highly heritable. Maladaptive levels of certain traits may be acquired as a result of anoxic or traumatic brain injury, neurodegenerative diseases such as Parkinson's disease, neurotoxicity such as lead exposure, bacterial infection such as Lyme disease or *Toxoplasmosis gondii*, as well as hormonal influences. While studies are still continuing via the use of various imaging techniques such as MRI, these traits have been shown to originate in various regions of the brain, such as amygdala and the prefrontal cortex [31,32,33]. Disorders in the prefrontal cortex and the executive functioning system have been shown to affect eating disorders [34]. Several studies have found that personality traits such as impulsivity, novelty seeking, stress reactivity, harm avoidance, perfectionism, and other personality traits are common in patients with eating disorders. Most of these studies assessed personality traits in their subjects during illness. Therefore, their personality traits could be a reflection of adverse effects of starvation [35].

Child abuse which encompasses physical, psychological and sexual abuse, as well as neglect has been shown innumerable studies to be precipitating factor in a wide variety of psychiatric disorders. Child abuse and neglect can cause profound changes in both the psychological structure and the neurochemistry of the development of the developing brain. In a study in New Zealand 25% of the study subjects in foster care exhibited an eating disorder (Tarren-Sweeney M 2006). An unstable home environment is detrimental to the emotional well-being of children, even in the absence of blatant abuse or neglect the stress of an unstable home can contribute to the development of an eating disorder [36,37].

Peer influence. In one study 40% of 9- and 10 year old girls are already trying to lose weight. Such dieting is reported to be influenced by peer behavior, with many of those individuals on a diet reporting their

friends also were dieting. The number of friends dieting and the number of friends who pressured them to diet also played a significant role in their own choices [38,39].

Socioeconomic status (SES) has been viewed as a risk factor for eating disorders, presuming that possessing more resources allows for an individual to actively choose to diet and reduce body weight [40]. The media plays a major role in the way in which people view themselves. Countless magazine ads and commercials depict rail thin celebrities like Lindsay Lohan, Nicole Richie, and Mary Kate Olsen, who appear to gain nothing but attention for their looks. Society has taught people that being accepted by others is necessary at all cost.[41]. Unfortunately this has led to the belief that in order to fit in one must look a certain way. Televised beauty competition such as Miss America Competition contributes to the idea of what it means to be beautiful because competitors are evaluated on the basis of their opinion [42].

Influence of western culture. Exposure to western culture that values slim body for women is presumed to play an important role in the increased eating disorders worldwide. Rate of eating disorders in countries such as Japan, Iran, and Singapore continues to increase among women have been exposed to western culture through temporary living in western countries for education, or even short-time vacation or through mass media [43,10]. Increase in the rate of eating disorders in populations exposed to western culture in those countries could strongly support the role of western culture in the development of eating disorders. Study of effects of western culture in relation to incidence of eating disorders in non-western immigrant women and girls has been recently given special attention [44,]. Most of the studies failed to control at least one variable such as socioeconomic status especially family income, which may have a positive correlation with body dissatisfaction, age difference, despite strong link between age and eating disorders[45]. Use of English language at home and religion could also be a potential cause of higher tendency for thinking about dieting and body shape, and as an indicator of acculturation[46,47]. Rikani and colleagues contend that a large population of immigrants in Canada coming from non-western countries provides an excellent opportunity to study influences of western culture on different ethnic origins with different religious affiliations socioeconomic status and eating habits[2].

III. Pathophysiology

Eating disorders like anorexia, bulimia, obesity and hedonic food perception are the most common eating disorders. The brain-gut axis is an important regulator of eating behavior, with specific biochemical signals involved in hunger, satiety food reward and metabolism. Norepinephrine and neuropeptide Y are involved in hunger signals; dopamine and opioids in food reward signals; serotonin, histamine and cholecystokinin (CCK) in satiety signals and leptin in metabolic signaling [48]. The dorsomedial thalamic tract is important in smell and taste sensation[49]. Anorexia nervosa and bulimia nervosa can occur with other psychiatric disorders, such as obsessive-compulsive disorder and hypnotic susceptibility [50,51]. Anorexia and loss of appetite can also occur secondarily to dialysis, pancreatic cancer, inflammation, renal and liver failure, and malnutrition [52-54]. Elevated cerebrospinal fluid (CSF) tryptophan correlates to the induction of cancer associated anorexia[55]. The histaminergic system of the hypothalamic-pituitary-adrenal (HPA) axis is important to the regulation of food intake; HI receptor agonist can reduce food seeking behavior; whereas, HI receptor antagonists like doxepin, cyprohepadine and promazine induce feeding[56]. Bulimia is a binge eating disorder with subsequent episodes of vomiting. Comorbid patients with obesity and bulimia show somatic behavioral and psychological impairment [57]. Repeated bingeing leads to increased gastric capacity, delayed emptying and blunted postprandial CCK –mediated satiety signal[58]. Bulimia can also occur secondary to diabetes and esophageal cancer[59]. In obese patients decreased plasma catecholamine correlate to carbohydrate preferences. Serum elevation of β endorphin and CCK found in obesity's leptin concentrations are also increased [60].

Eating behavior is a complex process controlled by the neuroendocrine system, of which the Hypothalamus-pituitary-adrenal-axis (HPA axis) is a major component. Dysregulation of the HPA axis has been associated with eating disorders[61] such as irregularities in the manufacture, amount or transmission of certain neurotransmitters, hormones, or neuropeptides and amino acids such as homocysteine, elevated levels of which are found in anorexia nervosa (AN) and bulimia nervosa (BN)[62-64]. Serotonin –a neurotransmitter involved in depression with inhibitory effect on eating behavior[65]. Dopamine a precursor of norepinephrine and epinephrine a neurotransmitter which regulates the rewarding property of food[66]. Norepinephrine is both a neurotransmitter and hormone may affect eating behavior[67]. Neuropeptide Y also known as NPY is a hormone that encourages eating and decreases metabolic rate[68]. Leptin and ghrelin-hormone leptin has an inhibitory effect on appetite by inducing a feeling of satiety, whereas ghrelin is appetite inducing hormone produced in the stomach and upper portion of the small intestine. While often associated with obesity, both hormones and their respective effects have implicated in the pathophysiology of anorexia nervosa and bulimia nervosa [69].

Bacterial role in the eating disorders. Studies on gut bacteria and immune system have shown that a majority of patients with anorexia nervosa and bulimia nervosa have elevated levels of autoantibodies that affect hormones and neuropeptides that regulates appetite control and stress response. There may be a direct correlation between autoantibodies levels and associated psychological traits [70]. Later study revealed that

autoantibodies reactive with alpha-MSH are, in fact generated against ClpB, protein produced by certain gut bacteria e.g., *Escherichia coli*. ClpB protein was identified as a conformational antigen-mimetic of alpha-MSH. In patients with eating disorders plasma levels of anti-ClpB IgG and IgM correlated with patient's psychological traits [71].

Pediatric Autoimmune Neuropsychiatric Disorders (PANDAS) associated with Streptococcal infection. Children with PANDAS have obsessive-compulsive disorder (OCD) and/or tic disorder such as Tourette syndrome, and whom symptoms worsen following infections such as "strep throat" (Streptococcal sore throat) or scarlet fever (NIMH). There is a possibility that PANDAS may be precipitating factor in the development of anorexia nervosa in some cases (PANDAS AN) [72]. Other factors in eating disorders include lesions to the right temporal lobe can cause pathological symptoms of DE, tumors in various regions of the brain have been implicated in abnormal eating patterns, brain calcification of the right thalamus have contributed to the development of AN [73-75]. Studies on starvation symptom suggest that symptoms of eating disorders are actually symptoms of starvation itself, not of a mental disorder [68].

IV. Clinical manifestations

Clinical manifestations varies according to the nature and severity of the eating disorder [76]. Some physical symptoms of eating disorders are weakness, fatigue, sensitivity to cold, reduced beard growth in men, reduction in waking up erection, reduced libido, weight loss and failure of growth [14]. Unexplained hoarseness may be a symptom of an underlying eating disorder, as the result of acid reflux, or entry of acidic gastric material into the laryngoesophageal tract. Patients who induce vomiting, such as those with anorexia nervosa, binge eating-purging type or those with purging-type bulimia nervosa are at risk for acid reflux [77]. Polycystic ovary syndrome (PCOS) is the most common endocrine disorder to affect women. Though often associated with obesity it can occur in normal weight individuals. PCOS has been associated with binge eating and bulimic behavior [78]. Other medical complications include, anemia, endocrine system dysfunction, electrolyte disturbances and cardiovascular diseases accompany eating disorders. Severity of medical complications depend on speed of weight loss, severity of underweight, duration of eating disorder, age of patients, and the intensity of purging [79].

V. Diagnosis

The medical history is the most powerful tool for diagnosing eating disorders [80]. All organic causes should be ruled out prior to a diagnosis of an eating disorder or other psychiatric disorder. Many patients present with subthreshold expressions of the two main diagnoses: other with different patterns and symptoms [81]. Neuroimaging using MRI, PET and SPECT scans have been used to detect cases in which a lesion, tumor or other organism condition has been either the sole causative or contributory factor in an eating disorder. Right frontal intracerebral lesions with their close relationship to limbic system could be causative for eating disorders, intracranial pathology should also be considered however certain is the diagnosis of early-onset anorexia nervosa. Second neuroimaging plays an important part in diagnosing early-onset anorexia nervosa, both from a clinical and a research prospective [82,83]. Psychological assessment by employing psychometric tests are important.

Many medical conditions may be contributory factors in the eating disorders that include: (a) disorder of adrenal cortex (Addison disease) may mimic many of the symptoms of anorexia nervosa (b) hypothyroidism, may mimic or be masked by or exacerbate an eating disorder (c) lupus erythematosus (SLE) have associated with many psychiatric disorders (d) Complications due to gastric adenocarcinoma have been misdiagnosed as an eating disorder [84-87].

Many bacterial, parasitic, and spirochetal infections are also predisposing factors in eating disorders that include (i) *Helicobacter pylori* which causes gastritis, gastric ulcer and stomach carcinoma. It also has an effect on circulating levels of leptin and ghrelin, two hormones which help regulate appetite (ii) *Toxoplasmosis* - in reported studies antidepressant treatment improved after adequate treatment for toxoplasma (iii) Lyme disease - it may be present as a variety of psychiatric or neurological disorder (iv) neurosyphilis can present with psychiatric symptoms alone. There may be up to one million cases of untreated syphilis in the U.S alone [88,86,89,90].

VI. Treatment, Prognosis and Prevention

Adequate psychotherapeutic treatments are still lacking due to complex treatment outcome variables. Fluoxetine can reduce vomiting and bingeing in 19% of bulimics, and the testosterone receptor antagonist, flutamide might also be effective [48,91]. Frequently used treatments include cognitive behavioral therapy (CBT), cognitive emotional behavioral therapy (CEBT), nutritional counselling, and medical nutritional counselling [92-95]. Orlistat is used in obesity treatment, and Olanzapine seems to promote weight gain [96]. People hospitalized with anorexia nervosa may be discharged while still underweight, resulting in relapse and re-hospitalization [97].

Prognosis estimates are complicated by non-uniform criteria used by various studies, for anorexia nervosa and bulimia recovery rates are in the 50% to 85% range, with larger proportions of people experiencing at least partial remission [98].

Mortality. A study by Sullivan showed that anorexia nervosa has the highest mortality rate of any other mental illnesses. It is estimated that 10% of people with anorexia nervosa die within 10 years of the onset of the disorder [99]. A recent Canadian study that assessed 326 patients diagnosed with anorexia nervosa for 20 years showed a higher mortality for anorexia nervosa than normal population [100].

Prevention aims to promote a healthy development before the occurrence of eating disorders. It also intends early identification of an eating disorder before it is too late to treat [101]. Internet and modern technologies provide new opportunities for prevention. on-line programs have the potential to increase the use of prevention programs ,at minimal cost[102].

VII. Conclusion

In eating disorders many medical conditions, genetic variance, psychiatric factors, bacterial, and parasitic infections are contributory factors. PA publication DSM-V guidelines are controversial. Efficacious psychotherapeutic treatments are still lacking. Common drugs used include fluoxetine, flutamide, orlistat and olanzapine. On-line prevention programs are beneficial.

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