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#### <u>General</u>

## Koro Syndrome: Epidemiology, Psychiatric and Physical Risk Factors, Clinical Presentation, Diagnosis, and Treatment Options

Yukino N. Strong<sup>1a</sup>, David Y. Cao<sup>1</sup>, Jessica Zhou<sup>1</sup>, Maya A. Guenther<sup>1</sup>, Danyon J. Anderson<sup>1</sup>, Alan D. Kaye<sup>2</sup>, Brian E. Blick<sup>2</sup>, Prathima R. Anandi<sup>2</sup>, Hirni Y. Patel<sup>2</sup>, Ivan Urits<sup>3</sup>

<sup>1</sup> School of Medicine, Medical College of Wisconsin, <sup>2</sup> Department of Anesthesiology, Louisiana State University Health, <sup>3</sup> SouthCoast Health

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Koro syndrome is a multi-tiered disease presenting as an overwhelming belief that one's sex organs are shrinking into their body. Moderate to severe anxiety attacks are associated with the condition, along with a fear of imminent death. Koro is often culturally related and is most seen as an epidemic form in East and Southeast Asia, although it can present anywhere worldwide in its sporadic form. The condition typically affects young males who believe in sex-related myths, and many individuals can co-present with anxiety, depression, or even psychosis. Although most presentations of Koro are self-limiting, the condition is harmful for one's self-esteem and quality of life, and some individuals may go through extreme, physically injurious measures to prevent genital retraction. Treatments include the use of psychotherapy that has a sex education component, especially if the patient believes in culturally rooted myths. In sporadic Koro, it is believed that if the primary psychiatric disorder is treated with anxiolytics, antidepressants, sedatives, or psychotics, the secondary Koro-like symptoms will also fade. Additional investigation on the prevalence, pathogenesis, factors that correlate with treatment efficacy are needed to fully understand Koro syndrome.

#### INTRODUCTION

Koro syndrome is a psychiatric disorder characterized by an intense fear of one's genitals retracting into their body, the result of which is fatal.<sup>1</sup> For men, there is a fear of the penis shrinking into the abdomen, and for women, there is a fear of the vulva and breasts shrinking into the abdomen and chest—all followed by impending death.<sup>2</sup> Although origins of the word Koro are uncertain, it is believed to be derived from a Malay word *kura* which means the head of a turtle, known to retract into their shell.<sup>1</sup>

There are two classifications of Koro: an endemic, culture-related type epidemic in parts of East and Southeast Asia and a sporadic, non-cultural type appearing throughout the rest of the world.<sup>1</sup> Epidemic Koro is considered culture-related due to beliefs rooted in historical literature or folklore,<sup>1</sup> and presents with classical, primary Koro symptoms such as deep, panic-like anxiety over penis retraction with fear of impending death.<sup>3</sup> Sporadic Koro—also known as Koro-like syndrome—does not have a cultural tie, and symptoms (genital shrinking without belief of resultant death) are usually secondary to schizophrenia, affective or medical disorders, and even recreational drug use.<sup>3</sup>

Although the pathogenesis of Koro is unclear, it is known that education, age, gender, and marital status are considered as risk factors.<sup>4</sup> Notably, Koro epidemics can occur through proliferation of fears, opinions, and rumors through news and media,<sup>1</sup> and the clinical course (lasting from days to months) is usually self-limiting.<sup>5</sup> A variety of treatment options—from education or counseling to medications—can be employed if Koro or Koro-like symptoms are chronic, recurrent, or related to a primary psychiatric or medical disorder.<sup>1</sup>

This review provides details of the most recent literature on Koro syndrome, highlighting the epidemiology, psychiatric and physical risk factors, clinical presentation, diagnosis, and treatment options for this condition. Since Koro appears worldwide but is often overlooked in North America, awareness of this rare syndrome as a differential di-

 a Corresponding author: Yuki Strong Medical College of Wisconsin School of Medicine 8701 W Watertown Plank Rd Milwaukee, WI 53226 ystrong@mcw.edu agnosis will be beneficial in providing timely and effective treatment for patients. In addition, shedding light on Koro will highlight the need for standardization of classification and measures of treatment outcomes so we can fully understand the extent and prevalence of Koro worldwide.

#### EPIDEMIOLOGY

Koro syndrome has an unclear incidence related to the condition's rarity. Additional classifications (epidemic, culture-related type versus sporadic, non-cultural type)<sup>1</sup> with stratifications (primary versus secondary)<sup>5</sup> complicate calculating an exact incidence of Koro worldwide. The condition can present in individuals of any age or gender, and tends to affect men who are younger than 30 years old.<sup>2</sup> Injury and deaths from Koro are rare, stemming from individuals resorting to physical methods in order to prevent genital retraction.<sup>6</sup> There have been no fewer than 12 epidemics of Koro reported in English literature between 1969 and 2017, totaling 1885 cases.<sup>7,8</sup> Interestingly, men are disproportionately affected by Koro syndrome, with on average only 9.2% of epidemic cases affecting females.<sup>8</sup>

Epidemic, culture-related Koro is reported to be common in parts of East and Southeast Asia, specifically in India, China, Malaysia, Indonesia, and Singapore,<sup>9</sup> as well as in West Africa.<sup>8</sup> The prevalence of epidemic Koro was once highest in China since there was a series of seven Koro outbursts occurring in 1948, 1955, 1966, 1974, 1984, 1985, and 1987-with the 1984-1985 epidemics notably affecting more than 3,000 people in 16 cities across the mainland.<sup>9</sup> Since the final 1987 epidemic, mental health campaigns and improvement of local economic conditions have allowed Koro to fade in China.<sup>9</sup> Now, Koro has been most common in India, with the past four epidemics occurring since 2010 affecting about 250 people.<sup>7,10</sup> However, the apparent prevalence of Koro epidemics in India within the past decade could be due to better clinical classification of the syndrome and reporting in literature within the countrv.

Sporadic Koro cases not related to culture have been reported worldwide across the continents of North America, Europe, Africa, Australia, and Asia; for instance, Turkey,<sup>11</sup> Portugal,<sup>12</sup> Greece,<sup>5</sup> Italy,<sup>13</sup> United States,<sup>14</sup> Mexico,<sup>15</sup> and Canada,<sup>16</sup> among others. Sporadic, non-cultural Koro is seen to be rarer than epidemic Koro, with only about 116 case reports published between 1967 and 2021.<sup>2,7</sup> The number of sporadic Koro cases may be underreported due to their association with primary psychiatric disorders (such as schizophrenia, depression, or anxiety), drug use, or other medical conditions—as well as difficulty with precisely characterizing symptoms for a diagnosis.<sup>3</sup>

# PSYCHIATRIC RISK FACTORS AND COMORBIDITIES

Risk factors for Koro syndrome where there are cultural myths about Koro include anxiety, cultural attitudes and beliefs, feelings of inadequate masculinity, and rumors about Koro in the environment.<sup>4,7</sup> In southern China where Koro is prevalent as a cultural myth, there is an overrepresentation of Koro syndrome reported in men under 24 years old.<sup>4</sup> Western case studies report patients with Koro-like symptoms secondary to neuropsychiatric disorders such as schizophrenia, obsessive-compulsive disorder, and major depression.<sup>15,17,18</sup> Koro syndrome was also reported in a patient who had mild cognitive impairment due to Alzheimer's disease<sup>19</sup> and another patient with a non-dominant temporoparietal stroke.<sup>20</sup> In the West, among Caucasian males, several cases have been reported of elderly men who developed Koro syndrome along with a neuropsychiatric disorder which indicate that having a neuropsychiatric disorder could be a risk factor for Koro syndrome. Females are also at risk for Koro syndrome although it is much less prevalent than in males and may be accompanied by psychosexual guilt.<sup>7</sup>

#### PHYSICAL RISK FACTORS AND COMORBIDITIES

Physical risk factors and comorbidities for Koro syndrome usually involve dysfunction of the genitals or the urogenital system. Infertility, a tumor of the corpus callosum, and ure-throcutaneous fistula all lead to secondary Koro syndrome in males.<sup>21-23</sup> Genital pain was also associated with fear of genital retraction in a patient who was diagnosed with anxiety disorder and Koro syndrome.<sup>24</sup> Two examples of drug-induced Koro syndrome have also been reported in a case involving cannabis and alcohol-induced hepatitis.<sup>25,26</sup> The example of alcoholic hepatitis induced Koro syndrome also involved a urinary tract infection which is consistent with other physical risk factors involving problems with the urogenital system.<sup>26</sup>

#### CLINICAL PRESENTATION AND DIAGNOSIS

Koro syndrome is characterized by a person's acute anxiety attacks due to their overwhelming belief that their sex organs are retracting and disappearing into their body and that this retraction is fatal, despite the lack of actual physical changes to these organs.<sup>27</sup> Individual episodes of these anxiety attacks usually last several hours but can persist for as long as 2 days.<sup>28</sup> Chronic sufferers of Koro can experience these episodes for decades. There have been reports of koro patients simultaneously experiencing psychotic depression, and Koro symptoms are highly likely to lower patients' self-esteem and overall mental wellbeing.<sup>29,30</sup> Diagnosis of Koro consists of both psychological evaluation and physical examination of the genital organs, the latter of which is used to rule out physical disorders such as hypospadias or measurable, sustained genital retraction.<sup>28,31</sup> The major diagnostic criteria are patients' report of genital (i.e. penis) retraction despite objective evidence, subsequent fear and anxiety, and physical attempts to prevent or reverse the retraction.<sup>9</sup> Some Koro patients report feeling weak and experiencing insomnia, as well as excessively measuring their penis size and attempting to physically pull their penis further out of their abdomen.

#### MANAGEMENT

Treatment and management of Koro syndrome and its associated symptoms involve a combination of medical, psychological, and social interventions.<sup>29</sup> This is in accordance with the multifactorial theories of Koro etiology, as it is proposed to have physical and cultural components.<sup>32</sup> Our knowledge of what treatments are effective is limited to the few case reports found in literature. Anxiolytics, antidepressants, sedatives, or antipsychotics are prescribed based on patients' co-presenting psychiatric conditions if applicable, because improvement in these psychiatric conditions is often associated with dissolution of Koro symptoms.<sup>1,33</sup> For example, one case report in Greece was treated for underlying anxiety, sleep disturbances, and psychosis with a combination of 20 mg citalopram and 200 mg quetiapine daily.<sup>5</sup> Another case addressed in the same paper had comorbid schizophrenia and a history of sexual trauma.<sup>5</sup> This patient was treated with 30 mg olanzapine daily and supportive psychotherapy aimed at decreasing feelings of guilt. His koro-like symptoms abated after three weeks of this treatment.<sup>5</sup> An 18-year-old Muslim male who was discovered to have comorbid OCD during treatment had his regimen changed to 150 mg sertraline daily, 0.5 mg clonazepam three times daily, and supportive psychotherapy. Once the treatment had been adjusted to target his OCD, his Koro syndrome improved within a month.<sup>10</sup> Similarly, a patient whose Koro syndrome seemed to be most associated with major depressive disorder achieved cessation of symptoms when treated with a combination of 150 mg trimipramine and bromazepam, along with supportive psychotherapy.<sup>33</sup> In yet another case report of an Italian male, after a one month regimen of 150 mg venlafaxine, 20 mg olanzapine, and 7.5 mg lorazepam, his delusional ideation and depression decreased, as demonstrated by reduced scores on measures such as the Brief Psychiatric Rating Scale (BPRS).<sup>13</sup> A patient with hypochondriasis and genital pain was treated with 125 mg desipramine daily and refused psychotherapy referral; his perception of genital retraction disappeared

after two weeks, and his presenting symptom of genital pain resolved three weeks after that.<sup>24</sup> Other treatments directed at underlying psychopathology have included haloperidol (aimed at psychosis)<sup>23</sup> and electroconvulsive therapy (when the syndrome was secondary to a tumor of the corpus callosum).<sup>22</sup>

Psychotherapy is crucial and should be paired with respectful education, where physicians counsel patients on their knowledge and understanding of sex organs and other sex-related topics, and navigate through any culturally rooted myths.<sup>1</sup> The majority of case reports involved supportive psychotherapy as a means of decreasing the guilt that is often deeply associated with Koro syndrome.<sup>5,33</sup>

Some patients may not improve despite these treatments.<sup>27</sup> This was found to be the case in two patients with chronic Koro syndrome. Both had been treated with the usual anxiolytics, sedatives, antidepressants, antipsychotics, and psychotherapies but had no remission of symptoms for 12 and 15 years respectively.<sup>27</sup>

#### CONCLUSION

Although epidemic Koro syndrome may be most common in parts of East and Southeast Asia, sporadic Koro can present anywhere worldwide.<sup>1</sup> Tackling both types of Koro will take a multi-pronged approach, pairing education and psychotherapy with anxiolytics or antidepressants when there is an associated psychiatric condition present.<sup>6</sup> Efforts to further elucidate the pathogenesis and prevalence of Koro syndrome should be explored, along with measures of treatment option efficacy. From those findings, a standardized treatment method based on varying Koro or Koro-like symptoms can be developed to ensure patients can recover from the debilitating anxiety associated with the syndrome. In the meantime, Koro syndrome should be kept as a differential diagnosis when patients present with hysteria relating to genital shrinkage.

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