Kleine-Levin Syndrome
An Overview and Relevance to Nursing Practice
Jacqueline M. Arnone, MSN, RN; and Richard P. Conti, PhD

ABSTRACT
Kleine-Levin syndrome (KLS) is a neuropsychiatric sleep disorder primarily affecting adolescent males. Onset is insidious, idiopathic, and hastened by neurological incident or infection. Typically, the initial onset occurs during the teen years or after the second decade, although cases have been documented in early childhood, adulthood, and senescence. KLS is marked by unexpected debilitating, yet reversible, episodic hypersomnia, with varying recurrence rates; cognitive and behavioral impairment; compulsive eating; and feelings of derealization, hypersexuality, apathy, and depressed mood. Diagnosis is problematic due to the syndrome’s rarity, disparity of presenting clinical symptoms, and misdiagnosis. Correct diagnosis can take up to 4 years. The clinical course is approximately 8 to 14 years from initial onset, yet may be longer in the adult form of the disorder. KLS has been shown to impact activities of daily living, usurping an adolescent of his/her social relations with peers, experiences, and time. [Journal of Psychosocial Nursing and Mental Health Services, 54(3), 41-47.]
Therefore, this partnership bestows a prospect for outreach to adolescent individuals with KLS for the professional nurse. The scope of nursing practice includes “diagnosing and treating human responses to actual or potential physical and emotional health problems, through such services as case finding, health teaching, [and] health counseling” (New Jersey Nurse Practice Act, 2006, p. 3), thereby making the professional nurse an important part of the health care team in caring for these clients and their families. For professional nurses in the acute and home care setting, to be able to meet the developmental and psychosocial needs of these clients and their families, knowledge regarding the psychosocial challenges and complications of KLS are warranted. Therefore, due to the dearth of studies regarding KLS in the nursing literature and the impact KLS has on adolescent clients and their families, the relevance to nursing practice and recommendations for future research are discussed.

**OVERVIEW**

KLS is a neuropsychiatric, atypical sleep disorder first termed more than 80 years ago (Critchley & Hoffman, 1942). The disease is also known as Rip Van Winkle or Sleeping Beauty syndrome (Lisk, 2009; Mudgal et al., 2014). It primarily affects adolescent males and is marked by repeated incidences of hypersomnia associated with varying degrees of behavioral and cognitive deviations (Arnulf et al., 2008; Geoffroy, Arnulf, Etain, & Henry, 2013). The KLS Foundation (2015, p. 4) stated:

At the onset of an episode the patient becomes progressively drowsy and sleeps for most of the day and night (hypersomnolence), sometimes waking only to eat or go to the bathroom. Each episode lasts days, weeks or months during which time all normal daily activities stop. Individuals are not able to care for themselves, or attend school and work.

Between periods of hypersomnia, individuals appear perfectly healthy, with no evidence of behavioral or physical dysfunction (Arnulf, Rico, & Mignot, 2012). Affected clients can proceed for weeks, months, or years, remaining asymptomatic between episodes, and then without warning, the symptoms reemerge (Dye, Jain, & Kothare, 2015). Affected individuals and their families live with the daily fear that another episode may ensue at any time (KLS Foundation, 2015). KLS episodes can continually reoccur for up to 10 years or longer, which poses potentially devastating effects on the lives of adolescent individuals and their families (KLS Foundation, 2015). Absence of an objective diagnostic test, may result in under-recognition and under-diagnosis of this disorder” (p. 575). Moreover, presenting clinical symptoms are psychiatric conditions or even intoxication, and therefore Arnulf et al. (2008) mused that this is why the disorder may not be initially suspected. To date, only case reports identifying single or several-person cases and retrospective systematic reviews of the aggregate documented cases have been published (Arnulf et al., 2008; Billiard, Jaussent, Dauvilliers, & Besset, 2011; Lachman, 2014; Shi, Tang, & Jiang, 2013).

**INCIDENCE AND PREVALENCE**

Mudgal et al. (2014) stated that the prevalence for KLS is unknown due to its sporadic presentation. Incidence rates are estimated at 1.5

...to meet the developmental and psychosocial needs of these clients and their families, knowledge regarding the psychosocial challenges and complications of Kleine-Levin syndrome are warranted.
cases per 1 million individuals, with the majority of documented cases found to occur more frequently in males (Arnulf et al., 2012). There is a higher incidence among Ashkenazi Jewish individuals in Israel (Gadoth et al., 2001), as well as American Jewish individuals (Arnulf et al., 2008), suggesting a potential founder effect for this population.

In a systematic review of 108 clients with KLS, Arnulf et al. (2008) reported finding that difficult births (i.e., prolonged labors, delayed or premature birth, and hypoxia) were revealed for 25% of affected clients. Moreover, they reported that 15% of patients stated being developmentally delayed. In addition, 34% of affected clients reported either one or both characteristics, compared to only 7% in the control group and parents (Arnulf et al., 2008). They also found that either probable or explicit genetic disorders were more prevalent in clients with KLS than in controls. Lastly, they noted that the recruited cases found within 1 year accounted for the greatest number of documented cases reported and was similar to the aggregate number of published documented cases already in the extant literature (Arnulf et al., 2008). They concluded that this finding implies the disorder may be more prevalent than previously believed (Arnulf et al., 2008).

PRECIPITATING FACTORS

Ramdurg (2010) stated that initial episodes of KLS were more frequently seen in autumn months (31.1%) or winter (31.1%), with a spike in December (14.8%). In addition, most clients demonstrated the ability to recall an incident that happened near initial onset of the disorder (Ramdurg, 2010). In a systematic review of 186 clients with KLS by Arnulf, Zeitzer, File, Farber, and Mignot (2005), most individuals reported experiencing infections (75%, with 25% stating cold-like symptoms with fever), followed by alcohol use (23%), sleep deprivation (22%), atypical stress (20%), physical exertion (19%), traveling (10%), trauma to the head (9%), and marijuana use (6%).

DIAGNOSIS

Diagnosis is problematic due to the syndrome’s rarity and vast disparity of presenting clinical symptoms (Mudgal et al., 2014). As a result, it can take up to 4 years for a correct diagnosis to be made (KLS Foundation, 2015). To date, no objective biochemical markers have been identified to assist early diagnosis of the disorder (Arnulf et al., 2012). Ramdurg (2010) noted episodes of somnolence, megaphagia, and subsequent retreat from normal activities of daily living can ape severe depression. Some case reports have also documented short-term high energy following sleep episodes, which mimic mania and therefore can cause a misdiagnosis of bipolar disorder. In addition, other mood disorders, narcolepsy, temporal lobe epilepsy, and multiple sclerosis share various symptoms of KLS, and therefore should be ruled out prior to making a final diagnosis (Ramdurg, 2010). The International Classification of Sleep Disorders-3 criteria (American Academy of Sleep Medicine, 2013) expressed five critical points for diagnosis:

A. At least two recurrent episodes of excessive sleepiness of 2 days to several weeks.
B. Episodes recur at least 1 per 18 months.
C. Normal alertness, cognitive function, behavior and mood between episodes.
D. At least one of these during an episode:
   • Cognitive dysfunction.
   • Altered perception, derealization.
   • Eating disorder (anorexia or hyperphagia).
   • Disinhibited behavior (such as hypersexuality).
E. Symptoms not better explained by other disorders. (p. 7)

Arnulf et al. (2012) stated that the initial sleep episode is often construed as an inexplicable infection, with symptoms resembling encephalitis or the flu. Additional associated events reported prior to onset include alcohol ingestion, sleep deprivation, stress, physical exhaustion, travel, brain trauma, surgeries (with local or general anesthesia), lactation, menstruation, and drug use (Arnulf et al., 2005; Arnulf et al., 2008; Lisk, 2009). Arnulf et al. (2012) added that the diagnosis of KLS is generally made only after the incidence of several episodes.

Episodic progression has been documented to begin rapidly after the causative event and can last from several days to months, although the latter is atypical (Arnulf et al., 2012). Cessation of these lengthened sleep cycles can occur just as quickly as they began. Overall, the clinical course of the disease averages 8 to 14 years from initial onset (typically by the third decade), yet the course can be longer in the adult form of the disorder (KLS Foundation, 2015).

Arnulf et al. (2012) stated:

Irrespective of age at onset, episodes during adulthood have less severe hypsomnia and start and end less suddenly than those in adolescence. More than 50% of cases that start before the age of 12 or after the age of 20 years remain unresolved after 25 years. (p. 919)

In addition, they reported the syndrome lasted approximately 13.6 years, with a range of 1 to 27 years, in 108 client cases reviewed, which resulted in incapacitation “for a mean of 8 months overall of 14 years” (Arnulf et al., 2008, p. 919). Individuals were only deemed “cured” if they did not experience an episode for >6 years (Lachman, 2014).

IMAGING STUDIES

Kas, Lavault, Habert, and Arnulf (2014) reported that the means to understanding the source of the diverse neuropsychiatric symptoms observed in KLS lies in performing functional imaging studies. Because symptoms of KLS may be related to the malfunction of the hypothalamus and thalamus (i.e., the parts of the brain that govern appetite and sleep), imaging studies have been conducted to observe these brain structures dur-
ing and in between sleep episodes (Engström, Hallböök, Szakacs, Karlsson, & Landtblom, 2014; Kas et al., 2014; Lo, Chou, & Yu, 2012). Arnulf et al. (2102) reported that magnetic resonance imaging and computerized tomography scans on clients with KLS demonstrated normal brain structure. Conversely, when a single-photon emission computerized tomography (SPECT) scan was used, there were pervasive defects noted in various areas of the brain. Findings included hypoperfusion of the right dorsomedial prefrontal cortex as well as the right parieto-temporal junction of the brain during sleep cycle episodes (Dye et al., 2015).

In addition, Kas et al. (2014) reported observed hypoperfusion in the thalamus, hypothalamus, cortical association region, and caudate during episodic events, with continuation occurring in between prolonged sleep episodes. One important finding using SPECT on clients in remission was that 56% demonstrated enduring hypoperfusion, which endorses chronic damage not substantiated in a post-follow-up examination (Vigren, Engström, & Landtblom, 2014). This finding supports persistent cognitive defects in an earlier study (Lo et al., 2012), which could be symbolic of a disease course that is more threatening than previously considered (Vigren et al., 2014).

Although the results of these imaging studies have been promising, the varying roles of the bilateral thalami in KLS remain ambiguous (Lo et al., 2012). However, dysfunction of the aforementioned neural structures has been shown to be a common thread among clients with KLS (Kas et al., 2014). Vigren et al. (2014) suggested using intraepisodal SPECT as an adjunctive imaging tool in the diagnosis of KLS, but not to be used alone for diagnosing the disorder, as the rate of sensitivity is decreased more so interepisodically than intraepisodically. Finally, as the majority of studies have arisen from single case reports, larger studies are necessary to establish if cognitive and psychiatric corollaries exist in between the prolonged sleep episodes, as well as in the long term (Arnulf et al., 2012; Kas et al., 2014).

BEHAVIORAL IMPAIRMENT

At first, symptoms of hypersomnia, hypersexuality, and hyperphagia were indicative of the main symptoms of KLS (Arnulf et al., 2005; Billiard et al., 2011). However, Arnulf et al. (2008) asserted occurrence of these symptoms existed in only approximately 45% of affected individuals. In addition, they stated that “although ‘positive’ symptoms such as irritability, aggressiveness, abnormal perception, increased eating, and sexuality were common, the overall impression was that of apathy, exhaustion, and dramatically increased sleep” (Arnulf et al., 2008, p. 484). Subsequent studies have pointed toward the occurrence of hypersonnia in addition to one of the diagnostic criteria set forth in the International Classification of Sleep Disorders-3 (American Academy of Sleep Medicine, 2013) as a more precise diagnostic framework for the disorder (Arnulf et al., 2012). Also, over the past 80 years, this disorder was thought to be benign in nature, as affected clients have been documented to return to a normal state in between sleep episodes, yet that posture has changed due to the capricious and precipitous disposition of the extended sleep cycles that affect the individual’s personal and social life (Arnulf et al., 2012). Billiard et al. (2011), in a systematic review of 339 cases of KLS, reported that compulsive eating was found in 100% of affected men and women. They noted some individuals reported this behavior from the onset of the disorder through the last cycle. They also found that this behavior occurred only during certain cycles, and was not consistent over time. Arnulf et al. (2008) noted clients reported craving sweets and uncommon food preferences during the hypomnolent period, eating “any and all food presented” (p. 485). Yet, they also reported one third of clients stated a decrease in appetite (Arnulf et al., 2008). In addition, due to the increased food intake during these episodes, clients were documented as gaining weight, resulting in an increase in body mass index, which Arnulf et al. (2008) stated could be indicative of a “core metabolic anomaly” (p. 489).

Sexual disinhibition in affected clients was more often recounted in men (50.7%) than women (29.1%) (Billiard et al., 2011). Billiard et al. (2011) mused that, for women, the disinhibition could take on a less perceptible manifestation, such as a “fantasy of being chatted up by men or experiencing love affairs” (p. 250). Arnulf et al. (2008) stated one half of their clients surveyed recounted an elevated sexual drive in at least a single cycle, yet some had a decreased sex drive; increased masturbation was noted to have occurred in one third of clients.

COGNITIVE IMPAIRMENT

Arnulf et al. (2012) stated all clients with KLS complained of apathy and impaired attentiveness, communication (both in discourse and reading), memory, and decision making. In addition, they reported clients being unable to multitask, demonstrating impaired muscle coordination, and having difficulty in tracking the passing of time (Arnulf et al., 2005; Arnulf et al., 2008). Furthermore, a distortion of the clients’ environment was also documented, which led to derealization, a feeling where their surroundings seemed not right, unnatural, or unreal (Arnulf et al., 2012; Ramdurg, 2010). Ramdurg (2010) also noted that, aside from the experience of derealization, some affected individuals reported auditory or visual hallucinations and paranoid delusions. Mild confusion was documented, yet affected clients were observed to be able to retain the ability to respond to difficult problems posed, as well as count, but at a slower speed than between prolonged sleep cycles (Arnulf et al., 2012).

Apathy was also observed in all clients, with adolescent individuals
terminating normal activities of daily living, such as calling or receiving telephone calls from their friends, seeing their friends, playing video games, wearing makeup, styling their hair, or bathing (Arnulf et al., 2012). Furthermore, clients were documented as appearing as if they were half asleep, sometimes fixing their eyelids shut, or looking unconcerned with dialogue when speaking to them in person (Arnulf et al., 2012).

Clients with long-term KLS have experienced hypoperfusion in different areas of the cerebral cortex, and documented cases of academic decline and deficits of auditory–verbal decline have been reported (Shi et al., 2013). Arnulf et al. (2005) noted the use of formal cognitive and memory tests found in their review of KLS cases was rare. However, when cognitive and memory tests were used, Arnulf et al. (2005) questioned the validity of the results due to the state of the client at the time the tests were conducted (e.g., they were uncooperative, sleepy, irritable, inattentive). Clients exhibited anterograde amnesia after the sleep episodes ended (Arnulf et al., 2012), and Arnulf et al. (2008) reported that only 13% of 108 clients with KLS were able to recount the events during the episodes in totality. However, clients returned to normalcy between the prolonged sleep cycles (Arnulf et al., 2005).

**TREATMENT**

Currently, no conclusive treatment for KLS exists (KLS Foundation, 2015). Treatment modalities for symptom abatement have thus far been palliative and differ between affected individuals (Arnulf et al., 2012). Oral stimulant drugs (i.e., amphetamine agents, methylphenidate, and modafinil) have been used to remedy lethargy, but may amplify irritability and will not improve cognitive abnormalities (National Institute of Neurological Disorders and Stroke, 2014). Because parallels have been drawn between KLS and particular mood disorders, lithium and carbamazepine have been used and, in some cases, demonstrated preventing additional episodes; however, Arnulf et al. (2008) reported their effects were “marginal, rare, and most case patients elected to abandon further use” (p. 492). Therefore, vigilance of clients in their homes during sleep episodes is recommended over pharmacotherapy (Arnulf et al., 2008; National Institute of Neurological Disorders and Stroke, 2014). In addition, supportive and educational measures have been suggested to be at the forefront of disease management for affected clients and their families (Arnulf et al., 2008).

**DISCUSSION AND FUTURE RECOMMENDATIONS**

KLS is a rare disorder that mainly affects adolescent males (approximately 70%) (National Institute of Neurological Disorders and Stroke, 2014), but has also been documented to present in childhood, adulthood, and senescence (Arnulf et al., 2012; Lachman, 2014). It is portrayed by periodic yet reversible cycles of excessive sleep that can persist from a few days to a few weeks (Dye et al., 2015). Incidence rates are estimated at 1.5 cases per 1 million individuals, with the majority of documented cases found to occur more frequently in males (Arnulf et al., 2012). There are approximately 700 documented cases of KLS globally, with approximately 500 in current studies whereby researchers and affected individuals hope to ascertain indications to cause and cure of the disorder (Borel, 2014).

Although researchers continue to look for answers to solve the many questions surrounding this multifaceted and mysterious disorder, it was discovered that there were two areas regarding KLS that lacked discussion in the literature. First, although several studies mentioned the impact and severity of disablement KLS has on adolescent individuals, there were no studies found regarding the psychosocial impact the disorder has on this cohort.

Interestingly, there were two studies found addressing this issue in regard to children and adolescent individuals diagnosed with narcolepsy. In the seminal study by Stores, Montgomery, and Wiggs (2006) on the psychosocial
problems (i.e., health-related qualities of life [HRQL]) of children with narcolepsy and those with excessive daytime sleepiness of unknown origin, they asserted:

Attempts to identify factors associated with poor psychosocial outcome in children with narcolepsy (eg, delay on diagnosis and misdiagnosis, possible adverse medication effects, and inappropriate reactions to the child’s symptoms of peers, parents, teachers and others) were frustrated by a lack of reliable retrospective information on these points. (p. 1122)

The same can be said for the availability of this particular data in the current literature regarding individuals with KLS. Stores et al. (2006) concluded that their results gave credence to the hypothesis that children with narcolepsy are at a greater risk for a wide spectrum of psychosocial difficulties.

Consequently, Inocente et al. (2014) conducted a study evaluating the HRQL on children and adolescent individuals with narcolepsy, based on the findings of Stores et al.'s (2006) initial work. They also concurred that children and adolescent individuals were not only at higher risk for poor HRQL, but also reported depressive symptoms, which demonstrated a strong bearing on HRQL (Inocente et al., 2014). Although narcolepsy is a different sleep disorder than KLS, there is a strong enough parallel between the two disorders to suggest that if there are psychosocial difficulties and depressive symptoms among children with narcolepsy, one could hypothesize similar findings in adolescent individuals with KLS.

To establish evidence-based practice guidelines in professional nursing practice, and in light of the dearth of studies investigating the psychosocial impact and quality of life issues within this cohort, a requisite exists for the examination of the adolescent individual’s lived experience with KLS. Moreover, a phenomenological study examining the client’s family is also warranted to ascertain their lived experience in caring for the client with KLS. This research will afford the professional nurse and interdisciplinary team with a greater clinical portrait of the issues and needs of not only the client, but also his/her family, both in the acute stage of the disorder and future.

NURSING IMPLICATIONS

Winger, Ekstedt, Wyller, and Helseth (2013) stated, “The general practitioner and the public health nurse might be the first persons who meet severely ill adolescents, and they need the knowledge to take action in an early stage of an illness” (p. 2655). In addition, physicians and nurses may care for adolescent individuals in their homes or the acute care setting during the various trajectories of the disease; devoting time to issues that matter to the clients will afford efficacy of effort and time (Winger et al., 2013). Arnone and Fitzsimons (2012) asserted, “Adolescents require developmentally appropriate and culturally specific information, psychologic and social support” (p. 253) More importantly, for this cohort, inclusion of a follow up that includes discussing physical and psychological effects of having KLS would be beneficial in planning care during the acute stage, as well as the future.

Winger et al. (2013) asserted adolescent individuals can “feel confirmed and experience relief and self-understanding” (p. 2655) when their stories are allowed to be verbalized. Moreover, trust can be facilitated through questions aimed at the issues of import to the adolescent and therefore foster a better relationship between the client, nurse, and health care team (Winger et al., 2013). With increased knowledge and understanding of the multifaceted nature of KLS, professional nurses can expand the adolescent individual’s and family’s knowledge through the promotion of client control and development of trust, and provide the adolescent individual with a dynamic and futuristic image of their worldview (Alligood & Tomey, 2006).

CONCLUSION

It is important for professional nurses, as integral partners of the interdisciplinary health care team, to understand the psychosocial challenges and complications of KLS and the potential impact the disease can have on the adolescent’s developmental trajectory. Furthermore, the dearth of qualitative research in the extant literature on the lived experience of this cohort and their families demonstrates a requisite for the commencement of qualitative studies to be generated that explore this phenomenon. Subsequent themes that evolve from such research will provide professional nurses and other health care providers the aptitude to render developmentally specific and culturally competent quality care through best practice that is restorative to and supportive of life and well-being for these clients and their families.

REFERENCES


Copyright © SLACK Incorporated