Cervical Ossification of the Posterior Longitudinal Ligament (OPLL) in Native Hawaiians and/or Polynesians: A 3-year Retrospective Demographic and Descriptive Pilot Study

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Abstract

Ossification of the posterior longitudinal ligament (OPLL) is a disease characterized by the replacement of the posterior longitudinal ligament with ectopic bone and cartilage. Historically, the disease was described as highly prevalent in Japanese and other Asian populations. However, recent studies suggest OPLL may have a higher prevalence in non-Asian communities than previously believed. To date, there are no demographic or epidemiologic studies examining OPLL in Native Hawaiian or Polynesian communities. The purpose of this study was to review the demographics and comorbidities of a cohort of patients with OPLL from the author's institution, designated as either Native Hawaiian and/or Polynesian (NHP) or Non-Native Hawaiian and/or Polynesian (NNHP). Demographic findings from this study were similar to previous literature demonstrating higher rates of OPLL in men and older patients with an average age of 56 years in the NHP group and 65 years in the NNHP group. There were no statistically significant differences in the rates of type II diabetes mellitus, coronary vascular disease, chronic kidney disease, or hypertension between NHP and NNHP groups. The NHP group exhibited statistically higher rates of obesity when compared to the NNHP group. Obesity's risk in the development or progression of OPLL in the NHP population has not been examined and requires additional investigation. This study serves as a beginning for further demographic and epidemiologic investigations into OPLL in Native Hawaiian and Polynesian communities to facilitate improved identification of those at risk and guide diagnosis and treatment of these patients.

Keywords

Ossification of posterior longitudinal ligament, Native Hawaiian, Polynesian, Spine

Acronyms and Abbreviations

CDC = Centers for Disease Control and Prevention
CKD = chronic kidney disease
CT = computed tomography
CT = computer tomography
CVD = coronary vascular disease
DMII = diabetes mellitus type II
HTN = hypertension
ICD-10 = International Classification of Disease-10
NHP = Native Hawaiian and/or Polynesian
NNHP = Non-Native Hawaiian and/or Polynesian (NNHP)
OPLL = ossification of the posterior longitudinal ligament
PLL = posterior longitudinal ligament

Introduction

Ossification of the posterior longitudinal ligament (OPLL) is a disease characterized by the replacement of the posterior longitudinal ligament (PLL)—the ligamentous tissue spanning the dorsal surface of the vertebral bodies—with ectopic bone and cartilage. The normal function of the PLL is to provide resistance against hyperflexion. This function becomes compromised in OPLL as proliferating fibroblast-like chondrocytes and osteoblasts disrupt the native ligament with cartilaginous tissues and form ossification and hyalinoid degeneration centers.[1,2] This pathologic process results in narrowing of the spinal canal, which can cause the symptoms of OPLL and lead to myelopathy, especially in the cervical spine.[3,4]

Upon presentation, 28% to 39% of patients will have clinical signs and symptoms of myelopathy.[5,6] OPLL is most frequently observed in the cervical spine, but rates of associated lesions at other spinal levels have been estimated to be as high as 56%.[7] Onset of OPLL is more common in men than women with a 2:1 or 3:1 ratio, with a predominance in the sixth or seventh decade of life.[6,8] Plain radiographs, dynamic imaging, computed tomography (CT), and magnetic resonance imaging are all critical in the initial workup of patients with OPLL. The Japanese Ministry of Public Health and Wellness classification system, based on a lateral radiograph, is the most commonly used classification system, but an axial CT is crucial for determining disease severity and canal compromise.[9] A study by Matsunaga, et al, demonstrated that the natural history of OPLL is related to the presence of myelopathy on initial presentation. In this study, 20% of patients without original myelopathy became myelopathic during the 17-year follow-up. At the 30-year follow-up, this number increased slightly to 29%.[6] If myelopathy is present upon initial exam, approximately 64% of patients may go on to further clinical deterioration and worsening myelopathy if conservative management is chosen.6 Prognosis worsens as symptoms worsen, with some estimates suggesting that 89% of patients with Nurick grade 3 or 4 myelopathy will progress towards confinement in a wheelchair or bed rest when treated conservatively.[3]

Treatment is determined by the degree of neurologic dysfunction. Conservative management is often reserved for patients with absent or mild symptoms, Nurick grade 1 or 2.[9] With

conservative management, worsening radiographic evidence of disease rates range from 42-58%, with increased risk of hospitalization for spinal cord injury.[3,4,10,11] Surgical treatment is considered the treatment of choice for patients with moderate to severe disease or progressively worsening myelopathic symptoms. As with other degenerative myelopathies, the goal of surgical treatment is decompression of the neural elements and maintenance, augmentation, and restoration of spinal alignment and biomechanical stability.[9]

As this disease was beginning to gain recognition and understanding, it was found to have a high incidence in Japan, resulting in a special commission for the investigation of the disease in 1975.[12] Once coined "The Japanese Disease," further epidemiologic studies of the disease have described demographic, clinical, and radiographic findings in other racial and ethnic groups, such as Whites, Blacks, non-Japanese Asians, and Hispanics.[13,14] The incidence rate varies from 0.8% to 4.6%, and prevalence of cervical OPLL between 0.6% to 6.3%, with rates varying based on ethnic groups being studied and the geographic locations of the studies.[8,15] Other studies have investigated associations with comorbid conditions such as diabetes, hypertension, cardiovascular disease, and renal disease.[8,16–20]

Spine surgeons at the authors' institution have anecdotally noted a relatively high incidence of OPLL in Native Hawaiian and/or Polynesian patients. To the authors' knowledge, there have been no studies examining the epidemiology of OPLL in these populations. This study aims to begin further demographic and epidemiologic investigations into OPLL in Native Hawaiian and Polynesian communities to facilitate improved identification of those at risk and guide the diagnosis and treatment of these patients.

Subjects and Methods

This study was a retrospective review of medical records from a level one trauma center in Hawai'i, from January 1, 2017, to December 31, 2019, totaling 3 years. Human Subjects Institutional Review Board approval was obtained, and strict adherence to the protocol was implemented.

All patients with an *International Classification of Disease-10, Tenth Edition* (ICD-10) code for cervical spondylopathies, and charts examined to identify a listed diagnosis of OPLL. These were identified over a 3-year period, which satisfied the inclusion criteria for the study. Patient's charts were then examined for exclusion criteria was limited to missing data regarding comorbid conditions documented in their electronic medical record and patients aged less than 18 years. All patients were then categorized by race and ethnicity as either Native Hawaiian and/or Polynesian (NHP) or Non-Native Hawaiian and/or Polynesian (NNHP). Race and ethnicities were self-reported by patients and were recorded in the electronic medical record. Additionally, comorbid conditions, such as diabetes mellitus type II (DMII), hypertension (HTN), chronic kidney disease (CKD), and coronary vascular disease (CVD), were chosen for investigation due to their inclusion in prior studies investigating comorbid conditions.[18,20–22] Their presence was determined based on a current ICD-10 coded diagnosis within each patient's chart. Furthermore, HTN was also assessed by determining if a patient's average systolic or diastolic blood pressure (in mm Hg), measured by the average of blood pressure readings during patient visits, met the American Heart Association's diagnostic criteria, which was a systolic blood pressure greater than 130 mm Hg and diastolic blood pressure greater than 80 mm Hg, respectively.[23] Obesity was determined by the presence of an active ICD-10 diagnosis code for obesity or an average body mass index (BMI) of 30 or greater, which is recognized as obesity by various health organizations such as the World Health Organization and the Centers for Disease Control and Prevention.[24,25]

Dependent variables included all comorbid conditions (No/Yes). The primary independent variable was race/ethnicity (NHP or NNHP). All independent and dependent variables above were considered dichotomous and coded and analyzed using IBM SPSS (Version 24). Normality of distribution analyses was conducted to assess skewness and kurtosis. A Welch's *t*-test was performed to determine if there was a statistically significant difference in average age between NHP and NNHP patients with OPLL. Data were found to be parametric, so therefore chi-square analyses were conducted. Results were considered significant at $P < .05$, with confidence intervals set at 95%.

Results

Demographics

A total of 138 patients met the inclusion criteria. Of the initial patients identified, 25 had missing demographic and descriptive data, and 1 was younger than 18 years. Of the 112 patients available for analysis, 29% were female (32 of 112), and 71% were male (80 of 112). There was no statistically significant difference between female and male distribution in NHP and NNHP patients with OPLL ($c^2 = 0.14$, $P = .70$, degree of freedom [df] = 1) as shown in Table 2. The average age at diagnosis was 61.6 years old for all patients. The average age within NHP patients was 56 years in NHP patients and 65 years in NNHP patients, with the difference in average age found to be statistically significant ($t = -3.90$, $P = .0002$). The NHP group comprised 34% (38 of 112) of the study group (Table 2).

Comorbid Conditions

Rates of comorbid conditions within NHP and NNHP groups can be found summarized in Table 1. There were no statistically significant differences in the rates of DMII ($c^2 = 1.44$, $P = .23$,

df = 1), CVD ($c^2 = 0.01$, $P = .93$, df = 1), HTN ($c^2 = 0.45$, $P = .50$, df = 1), or CKD ($c^2 = 0.05$, $P = .82$, df = 1) between NHP and NNHP in this study. NHP patients were statistically more likely to be obese when compared to NNHP patients ($c^2 = 14.68$, $P < 0.001$, df = 1). These findings are summarized in Table 2.

Table 1. Rates of Comorbid Conditions Among Native and Non-Native Hawaiian and/or Polynesian Patients With Ossification of the Posterior Longitudinal Ligament

	Native Hawaiian and/or Polynesian n= 38 (%)	Non-Native Hawaiian and/or Polynesian n= 74 (%)
DMII	22 (58%)	34 (46%)
CVD	9 (24%)	17 (23%)
CKD	9 (24%)	19 (26%)
Obesity	29 (76%)	30 (41%)
HTN	20 (53%)	34 (46%)

Abbreviations: CVD, coronaryvascular disease; CKD, chronic kidney disease; DMII, Diabetes mellitus type II; HTN, hypertension

Table 2. Demographic and Comorbid Conditions Among Native and Non-Native Hawaiian and/or Polynesian Patients with Ossification of the Posterior Longitudinal Ligament

	Native Hawaiian and/or Polynesian n= 38 (%)	Non-Native Hawaiian and/or Polynesian n= 74 (%)	*P*-value
Sex			
Female	10 (26%)	22 (70%)	.70
Male	28 (74%)	52 (30%)	
DMII			
Yes	22 (58%)	34 (46%)	.23
No	16 (42%)	40 (54%)	
CVD			
Yes	9 (24%)	17 (23%)	.93
No	29 (76%)	57 (77%)	
CKD			
Yes	9 (34%)	19 (76%)	.82
No	29 (26%)	55 (74%)	
Obesity			
Yes	29 (76%)	30 (40%)	.0001*
No	9 (24%)	44 (59%)	
HTN			
Yes	20 (53%)	34 (46%)	.5
No	18 (47%)	40 (54%)	

Abbreviations: CVD, coronary vascular disease; CKD, chronic kidney disease; DMII, Diabetes mellitus type II; HTN, hypertension.
*statistically significant

Discussion

Orthopedic spine and neurosurgeons at the authors' institution have anecdotally stated that there appears to be a high prevalence of OPLL within NHP communities. To date, there haven't been any demographic or descriptive studies of OPLL in NHP communities. Historically, the disease has been described as having a preponderance in Asians, but more recent research has suggested that the prevalence of OPLL is higher in other racial groups due to increased awareness and surveillance.[26,27] As such, this study stands as the first demographic or descriptive analysis of OPLL within NHP communities.

Previous studies have found that men are two to three times more likely to be diagnosed with cervical OPLL.[28,29] This study had similar results with an approximately 3:1 ratio of men to women in NNHP and NHP populations. The mean age of diagnosis in our study was 61.6 years in combined groups. These findings are similar to previous studies, which stated that patients with OPLL are generally between 50 to 60 years old, implying a degenerative nature to the disease process.[10,27,30] Interestingly, there was a statistically significant difference in average age between patient groups. This warrants further investigation into any potential risk factors contributing to the earlier development of disease within NHP patients and could prompt earlier and improved disease surveillance within NHP communities. In this study, 34% of the patients identified as NHP as compared to 27% of Hawai'i's population identifying as Native Hawaiian or other Pacific Islander in a recent survey, though this census data included populations that are not historically considered Polynesian.[31] The higher percentage of NHP patients in this study compared with Hawai'i's population demographics may suggest a correlation between OPLL and NHP race/ethnicity. A direct association could not be analyzed between race/ethnicity and OPLL in this study due to design. Any such relationship would require further analysis, including examining potentially confounding variables such as socioeconomic status or health care access.

In our small cohort, the NHP group had a statistically higher rate of obesity when compared to the NNHP group. However, our study's design does not allow for a direct cause and effect analysis. The link between obesity and OPLL remains unclear, but previous literature has suggested that obesity may lead to altered metabolism, upregulation of insulin, and concomitant biochemical homeostatic alterations. This may result in ectopic bone formation and OPLL, though the exact pathophysiologic mechanism has yet to be determined.[19,32,33] The 74% rate of obesity among the NHP group in this study is higher than the 52% of Native Hawaiian/Pacific Islander persons in the United States identified as obese.[34] This high rate of obesity in OPLL patients is consistent with previous literature focusing on other racial groups.[7,17,21,35–37] This relationship has never been examined in NHP populations, however.[19,21,36] Obesity rates have been reported to be higher in the NHP communities than other

ethnic groups, which may present as a confounding variable and would need to be controlled in future studies examining any association.[38,39] Other risk factors associated with OPLL include diet, genetic predisposition, and physical activity, which were not evaluated in this study due to the logistical challenges in obtaining this information retrospectively.[37,40–44]

There are limitations to this study. A significant limitation was the method by which race and ethnicity were determined. Hawai'i has the highest rate of multiracial residents in the United States.[45] This makes reporting on demographic data difficult due to the incredibly high ethnic and racial heterogeneity rates. It is possible that individuals did not report full racial or ethnic makeup or were simply unaware of it. In addition, although rates of obesity have been documented to be higher in the NHP populations compared to other racial or ethnic groups, it is important to recognize this observation is confounded by a complex interplay of socioeconomic factors and health care access.[2,10,39,46,47] Any future analysis between the link of obesity and OPLL should recognize these additional considerations. A related issue plaguing the comparison between NHP and NNHP groups is the lack of subset analysis between ethnically Japanese individuals. As mentioned, OPLL first gained notoriety as a "Japanese Disease." While it has been shown to have higher than believed prevalence in other populations, prior studies have shown it to have a higher prevalence than other Asian ethnic groups.[15] As such, it could be of interest in future studies to compare an NHP to a group of ethnically Japanese individuals living in Japan as well, in addition to a conglomerated NNHP group as done in this study.

Another limitation is the small sample size. The small sample size obtained in this study is not surprising given the low incidence of OPLL in the general population. It has also been suggested that the general incidence and prevalence may be underreported since many patients are asymptomatic or do not receive a proper diagnosis.[27] Additionally, this study evaluated patients diagnosed with cervical OPLL, which suggests patients with isolated thoracic or lumbar OPLL were not captured through cervical OPLL specific ICD-10 coding. There is also a possibility that NHP patients with cervical OPLL were not all captured due to improper ICD-10 coding. Likewise, this study identified individuals with OPLL by diagnosis in chart, without determining how symptomatic each individual was. In future studies, efforts should be made to determine which individuals with OPLL received treatment, abnormal physical findings, and clinical presentation for further subgroup analysis. Future research to further explore the true prevalence, relative risk, and association of comorbid conditions of OPLL in the NHP population would require a controlled cohort sample.

Conclusion

This study provides a novel demographic and descriptive analysis of NHP with a diagnosis of OPLL. This study reiterates reports of a higher prevalence of OPLL in men and older patients, which remained in subgroup analysis within the NHP population, though the average age of diagnosis was found to be younger in NHP patients. In addition, this study suggests NHP patients diagnosed with OPLL have statistically higher rates of obesity than NNHP patients, which may be determined to be a potential risk factor in future studies. The true epidemiology of OPLL in the NHP community remains unclear. Nevertheless, this pilot study provides valuable information for future prospective case-controlled analyses to investigate potential epidemiologic ties between OPLL and the NHP populations. In doing so, medical providers may better understand who is at risk, improve diagnostic capabilities, and optimally treat those within NHP communities.

Conflict of Interest

None of the authors identify a conflict of interest.

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References

1. Song J, Mizuno J, Hashizume Y, Nakagawa H. Immunohistochemistry of symptomatic hypertrophy of the posterior longitudinal ligament with special reference to ligamentous ossification. *Spinal Cord*. 2006;44(9):576-581. doi:10.1038/sj.sc.3101881
2. Yonemori K, Imamura T, Ishidou Y, et al. Bone morphogenetic protein receptors and activin receptors are highly expressed in ossified ligament tissues of patients with ossification of the posterior longitudinal ligament. *Am J Pathol*. 1997;150(4):1335-1347. https://pubmed.ncbi.nlm.nih.gov/9094990.
3. Matsunaga S, Sakou T, Taketomi E, Komiya S. Clinical course of patients with ossification of the posterior longitudinal ligament: a minimum 10-year cohort study. *J Neurosurg Spine*. 100(3):245-248. doi:10.3171/spi.2004.100.3.0245
4. Matsunaga S, Kukita M, Hayashi K, et al. Pathogenesis of myelopathy in patients with ossification of the posterior longitudinal ligament. *J Neurosurg Spine*. 96(2):168-172. doi:10.3171/spi.2002.96.2.0168
5. Chang H, Song KJ, Kim HY, Choi BW. Factors related to the development of myelopathy in patients with cervical ossification of the posterior longitudinal ligament. *J Bone Jt Surg - Ser B*. 2012;94 B(7):946-949. doi:10.1302/0301-620X.94B7.29018
6. Matsunaga S, Sakou T. Ossification of the posterior longitudinal ligament of the cervical spine: etiology and natural history. *Spine (Phila Pa 1976)*. 2012;37(5). https://journals.lww.com/spinejournal/Fulltext/2012/03010/Ossification_of_the_Posterior_Longitudinal.22.aspx.
7. Hirai T, Yoshii T, Iwanami A, et al. Prevalence and distribution of ossified lesions in the whole spine of patients with cervical ossification of the posterior longitudinal ligament: a multicenter study (JOSL CT study). *PLoS One*. 2016;11(8):e0160117-e0160117. doi:10.1371/journal.pone.0160117
8. Moon BJ, Choi SK, Shin DA, et al. Prevalence, incidence, comorbidity, and mortality rates of ossification of posterior longitudinal ligament in the cervical spine: A Nested Case-Control Cohort Study. *World Neurosurg*. 2018;117:e323-e328. doi:10.1016/j.wneu.2018.06.023

9. Head J, Rymarczuk G, Stricsek G, et al. Ossification of the posterior longitudinal ligament: surgical approaches and associated complications. *Neurospine*. 2019;16(3):517-529. doi:10.14245/ns.1938222.111
10. Inamasu J, Guiot BH, Sachs DC. Ossification of the posterior longitudinal ligament: An update on its biology, epidemiology, and natural history. *Neurosurgery*. 2006;58(6):1027-1039. doi:10.1227/01.NEU.0000215867.87770.73
11. Wu J-C, Chen Y-C, Liu L, et al. Conservatively treated ossification of the posterior longitudinal ligament increases the risk of spinal cord injury: A nationwide cohort study. *J Neurotrauma*. 2011;29(3):462-468. doi:10.1089/neu.2011.2095
12. TSUYAMAN. Ossification of the posterior longitudinal ligament of the spine. *Clin Orthop Relat Res*. 1984;184. https://journals.lww.com/clinorthop/Fulltext/1984/04000/Ossification_of_the_Posterior_Longitudinal.10.aspx.
13. Wang MY, Thambuswamy M. Ossification of the posterior longitudinal ligament in non-Asians: demographic, clinical, and radiographic findings in 43 patients. *Neurosurg Focus*. 2011;30(3):0-4. doi:10.3171/2010.12.FOCUS10277
14. Lee T, Chacha PB, Khoo J. Ossification of posterior longitudinal ligament of the cervical spine in non-Japanese Asians. *Surg Neurol*. 1991;35(1):40-44. doi:10.1016/0090-3019(91)90200-S
15. Liang H, Liu G, Lu S, et al. Epidemiology of ossification of the spinal ligaments and associated factors in the Chinese population: a cross-sectional study of 2000 consecutive individuals. *BMC Musculoskelet Disord*. 2019;20(1):253. doi:10.1186/s12891-019-2569-1
16. Shin J, Choi JY, Kim YW, Chang JS, Yoon SY. Quantification of risk Factors for cervical ossification of the posterior longitudinal ligament in Korean populations: A nationwide population-based case-control Study. *Spine (Phila Pa 1976)*. 2019;44(16):E957-E964. doi:10.1097/BRS.0000000000003027
17. Kobashi G, Washio M, Okamoto K, et al. High body mass index after age 20 and diabetes mellitus are independent risk factors for ossification of the posterior longitudinal ligament of the spine in Japanese Subjects: A case-control study in multiple hospitals. *Spine (Phila Pa 1976)*. 2004;29(9):1006-1010. doi:10.1097/00007632-200405010-00011
18. Wu JC, Liu L, Chen YC, Huang WC, Chen TJ, Cheng H. Ossification of the posterior longitudinal ligament in the cervical spine: An 11-year comprehensive national epidemiology study. *Neurosurg Focus*. 2011;30(3):1-3. doi:10.3171/2010.12.FOCUS10268
19. Akune T, Ogata N, Seichi A, Ohnishi I, Nakamura K, Kawaguchi H. Insulin secretory response is positively associated with the extent of ossification of the posterior longitudinal ligament of the spine. *J Bone Jt Surg - Ser A*. 2001;83(10):1537-1544. doi:10.2106/00004623-200110000-00013
20. Hashizume Y. PATHOLOGICAL STUDIES ON THE OSSIFICATION OF THE POSTERIOR LONGITUDINAL LIGAMENT (OPLL). 1980;30(2):255-273.
21. Endo T, Takahata M, Koike Y, Iwasaki N. Clinical characteristics of patients with thoracic myelopathy caused by ossification of the posterior longitudinal ligament. *J Bone Miner Metab*. 2020;38(1):63-69. doi:10.1007/s00774-019-01026-8
22. Jia J, Chen W, Xu L, Wu T, Cheng X. A modified laminoplasty technique to treat cervical myelopathy secondary to ossification of the posterior longitudinal ligament (OPLL). *Med Sci Monit*. 2017;23:4855-4864. doi:10.12659/MSM.902468
23. Carey R, Whelton P . Guideline for the prevention, detection, evaluation, and management of high blood pressure in adults: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Hypertension*. 2018;71(6):e13-e115. doi:10.1161/HYP.0000000000000065
24. World Health Organization. Obesity and overweight: factsheet. Available at: https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight. Published 2021. Accessed April 17, 2021.
25. Centers for Disease Control and Prevention. Defining adult overweight & obesity. Available at: https://www.cdc.gov/obesity/adult/defining.html. Published 2021. Accessed April 17, 2021.
26. Kalb S, Martirosyan NL, Perez-Orribo L, Kalani MYS, Theodore N. Analysis of demographics, risk factors, clinical presentation, and surgical treatment modalities for the ossified posterior longitudinal ligament. *Neurosurg Focus*. 2011;30(3):1-9. doi:10.3171/2010.12.FOCUS10265
27. Sasaki E, Ono A, Yokoyama T, et al. Prevalence and symptom of ossification of posterior longitudinal ligaments in the Japanese general population. *J Orthop Sci*. 2014;19(3):405-411. doi:10.1007/s00776-014-0552-0
28. Matsunaga S, Nakamura K, Seichi A, et al. Radiographic Predictors for the Development of Myelopathy in Patients With Ossification of the Posterior Longitudinal Ligament: A Multicenter Cohort Study. *Spine (Phila Pa 1976)*. 2008;33(24). https://journals.lww.com/spinejournal/Fulltext/2008/11150/Radiographic_Predictors_for_the_Development_of.13.aspx.
29. Mori K, Kasahara T, Mimura T, et al. Prevalence, distribution, and morphology of thoracic ossification of the yellow ligament in Japanese: results of CT-based cross-sectional study. *Spine (Phila Pa 1976)*. 2013;38(19):E1216-22. doi:10.1097/brs.0b013e31829e018b
30. Wu J-C, Liu L, Chen Y-C, Huang W-C, Chen T-J, Cheng H. Ossification of the posterior longitudinal ligament in the cervical spine: an 11-year comprehensive national epidemiology study. *Neurosurg Focus FOC*. 30(3):E5. doi:10.3171/2010.12.FOCUS10268
31. Hawaii State Department of Business ED and T-READ. Latest Population Estimate Data. https://census.hawaii.gov/home/population-estimate/. Published 2019. Accessed April 17, 2021.
32. Tsuru M, Ono A, Umeyama H, Takeuchi M, Nagata K. Ubiquitin-dependent proteolysis of CXCL7 leads to posterior longitudinal ligament ossification. *PLoS One*. 2018;13(5):1-23. doi:10.1371/journal.pone.0196204
33. Ikeda Y, Nakajima A, Aiba A, et al. Association between serum leptin and bone metabolic markers, and the development of heterotopic ossification of the spinal ligament in female patients with ossification of the posterior longitudinal ligament. *Eur Spine J*. 2011;20(9):1450-1458. doi:10.1007/s00586-011-1688-7
34. Centers for Disease Control and Prevention. Summary Health Statistics. National Health Interview Survey-table A-15a. https://www.cdc.gov/nchs/nhis/shs/tables.htm. Published 2016. Accessed April 17, 2021.
35. Nam DC, Lee HJ, Lee CJ, Hwang S. Molecular pathophysiology of ossification of the posterior longitudinal ligament (OPLL). 2019;27(4):342-348.
36. Shingyouchi Y, Nagahama A, Niida M. Ligamentous ossification of the cervical spine in the late middle-aged Japanese men: Its relation to body mass index and glucose metabolism. *Spine (Phila Pa 1976)*. 1996;21(21). https://journals.lww.com/spinejournal/Fulltext/1996/11010/Ligamentous_Ossification_of_the_Cervical_Spine_in.13.aspx.
37. Okamoto K, Kobashi G, Washio M, et al. Dietary habits and risk of ossification of the posterior longitudinal ligaments of the spine (OPLL); findings from a case-control study in Japan. *J Bone Miner Metab*. 2004;22(6):612-617. doi:10.1007/s00774-004-0531-1
38. Aluli NE. Prevalence of obesity in a Native Hawaiian population. *Am J Clin Nutr*. 1991;53(6):1556S-1560S. doi:10.1093/ajcn/53.6.1556S
39. McCubbin LD, Antonio M. Discrimination and obesity among Native Hawaiians. *Hawaii J Med Public Health*. 2012;71(12):346-352. https://pubmed.ncbi.nlm.nih.gov/23251872.
40. Niu C-C, Lin S-S, Yuan L-J, et al. Correlation of blood bone turnover biomarkers and Wnt signaling antagonists with AS, DISH, OPLL, and OYL. *BMC Musculoskelet Disord*. 2017;18(1):61. doi:10.1186/s12891-017-1425-4
41. Nakajima H, Watanabe S, Honjoh K, Okawa A, Matsumoto M, Matsumine A. Expression analysis of susceptibility genes for ossification of the posterior longitudinal ligament of the cervical spine in human OPLL-related tissues and a spinal hyperostotic mouse (ttw/ttw). *Spine (Phila Pa 1976)*. 2020;45(22):E1460-E1468. doi:10.1097/BRS.0000000000003648
42. Maeda S, Koga H, Matsunaga S, et al. Gender-specific haplotype association of collagen α2 (XI) gene in ossification of the posterior longitudinal ligament of the spine. *J Hum Genet*. 2001;46(1):1-4. doi:10.1007/s100380170117
43. Ren Y, Liu Z zhong, Feng J, et al. Association of a bmp9 haplotype with ossification of the posterior longitudinal ligament (OPLL) in a chinese population. *PLoS One*. 2012;7(7):3-9. doi:10.1371/journal.pone.0040587
44. Sohn S, Chung CK. Increased bone mineral density and decreased prevalence of osteoporosis in cervical ossification of the posterior longitudinal ligament: A case-control study. *Calcif Tissue Int*. 2013;92(1):28-34. doi:10.1007/s00223-012-9662-x
45. KROGSTAD JM. Hawaii is home to the nation's largest share of multiracial Americans. Pew Research Center.
46. Washio M, Kobashi G, Okamoto K, et al. Sleeping habit and other life styles in the prime of sife and risk for ossification of the posterior longitudinal ligament of the spine (OPLL): a Case-control study in Japan. *J Epidemiol*. 2004;14(5):168-173. doi:10.2188/jea.14.168
47. Uchima O, Wu YY, Browne C, Braun KL. Disparities in diabetes prevalence among native Hawaiians/Other Pacific Islanders and Asians in Hawai'i. *Prev Chronic Dis 16*. 16. https://stacks.cdc.gov/view/cdc/77106.