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Disparities in lower extremity amputation among Native Americans with diabetic foot ulcerations

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Background

It is a well-documented declaration that the Native American (NA)/American Indian (AI) population is disproportionately affected by many chronic conditions. Among the chronic and often fatal ailments, diabetes mellitus (DM) is a prevailing diagnosis [1]. According to the 2017 American Diabetes Association, DM is responsible for significant deaths and is a substantial cost to society at $327 billion USD in the United States (US) [2]. Complications of DM include peripheral artery disease (PAD), a macrovascular complication, and peripheral neuropathy (PN), a microvascular condition, which in turn cascade into other adverse health outcomes [3,4]. Impaired vascular flow and loss of sensitivity to the extremities, particularly to the feet, likewise increases risk of diabetic foot ulceration (DFU) [3,4]. As a consequence of an infected foot ulceration and subsequent osteomyelitis or gangrene, patients may undergo lower extremity amputation (LEA) [4,5]. DFU not only limits mobility and causes pain and discomfort, but foot ulceration may even increase mortality rates and reduce life expectancy [6,7]. The rate of recurrence for DFU within 1 year is roughly 40%, about 60% within 3 years, and 65% within 5 years [8].

Lower extremity amputation is 10 to 20 times more common in patients with PAD secondary to diabetes compared to non-diabetics, with up to 75% of LEAs being performed in these patients [9]. The opposite leg in up to 42% of diabetic patients is amputated within three years [10]. In 2010, 73,000 amputations were performed in diabetic patients, accounting for more than 50% of amputations in the US [4]. Mortality, quality of life, and physical function are significantly worst after major amputations (ankle and above) [3,11]. Approximately half of amputees will die within one year and as many as 70% of amputees have a 5-year mortality rate [11]. In addition, the cost to US healthcare payers due to DFUs and subsequent lower LEAs was estimated to be $11 billion USD in 2001 [12].

Minority populations such as NA, African Americans (AAs), and Hispanics are disproportionately affected by DM. According to the 2017 National Diabetes Statistics Report by the CDC, the NA population has the highest rate of prevalence of diabetes at 15.1%, followed by AAs with 12.7%, and Hispanics at 12.1%, while DM was prevalent in only 7.4% of non-Hispanic whites (whites) [13]. These same subgroups also experience more diabetes-related complications, such as PAD, DFUs, and LEAs [14-16]. NAs, AAs, and Hispanics likewise have higher rates of premature mortality as well as worse diabetes outcomes compared to whites [17,18]. It is estimated that American Indians (AIs) have four times higher mortality rate due to diabetes than that of the US general population [18]. Additionally, the rate for LEAs among NAs was greater than that of the general population [19]. The WHO Multinational Study of Vascular Disease in Diabetes from 2001 likewise established incidences of amputation secondary to DM of the NA population to be 31.0 and 9.7 per 1,000 persons, respectively [20]. Furthermore, NAs in the state of Arizona are at a higher risk of LEA [21]. Other minority groups such as AA and Hispanic patients are more likely to undergo a major LEA as opposed to limb salvage than whites [22].

The differences in outcomes and therapeutic approaches to a diabetic patient with a foot ulcer has been studied extensively in AAs and whites, yet what factors contribute to disparities in diabetes-related LEAs among the NA population remains unclear. With a projected population of 10.2 million individuals by 2060, it is imperative to understand and address inequalities of the NA population as it relates to their health [23]. This review seeks to ascertain elements leading to major LEAs among the NA population with DFUs. Among the significant factors leading to elevated risks of leg amputation that are included in this discussion are predisposing genetics, lifestyle behaviors, access to healthcare, socioeconomic status, patient attitude towards Western medicine, and healthcare provider bias.

Current State of Evidence

The review focuses on the NA population, referring to indigenous persons in the US of federally recognized tribal affiliation and including Alaskan Natives (AN). There are 573 NA tribes that are legally recognized by the Bureau of Indian affairs of the US as of July 2018, of which include 231 tribes located in Alaska [24]. While it may seem unreasonable to place all 573 tribes under one group and make generalizations, recent literature has indicated that all NA populations in North and South America derive from a single population [25]. Though each tribe may have its own unique customs, traditions, or even phenotypic features, NAs across all tribal affiliations share a common genotype [25].

Predisposing Genetics

The NA population is genetically predisposed to developing DM. Via genome-wide association studies (GWAS), recent literature has discovered more than 70 genomic regions in which single nucleotide polymorphisms (SNPs) are correlated with Type 2 DM. Of these regions, nine SNPs have been identified in AI and more specifically, the DNER

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locus conferred susceptibility for young-onset T2DM in Pima Indians of Arizona [26,27]. Additionally, other SNPs have been associated with higher 2-hour glucose concentrations, insulin resistance, lower acute insulin secretion, higher BMI, and higher percent body fat [28-31].

Native Americans are also modestly predisposed to developing PAD [32]. A recent study found a polymorphism of the gene encoding methylenetetrahydrofolate reductase (MTHFR) that is more prevalent of NAs of Oji-Cree descent [32]. While this gene has been linked to retinopathy, nephropathy, atherosclerosis, and coronary artery disease, this study determined the MTHFR 677C>T polymorphism also demonstrated a modest genetic influence on the development of PAD [32]. Another study found a common functional variant of the cholesterol transporter, ABCA1, that is exclusive to people of Native American populations, and is a major determinant of HDL-C levels as well as a higher BMI [33].

Lifestyle Behaviors

Researchers have delved into what lifestyle factors may be contributing to the development of DM and its consequences in the NA population. Native Americans have a higher prevalence of tobacco use, obesity and physical inactivity, binge-drinking, sugar-sweetened beverage consumption, high blood pressure, and report of fair or poor health status [1,34-36]. It has also been shown that compared with whites, NAs reported a lower prevalence of having a personal doctor or healthcare provider, fruit and vegetable consumption, cancer screening, and seatbelt use [34]. There is even data to suggest that mental illnesses such as depression disproportionately affects the NA population, which is also linked with worse glycemic control [37].

Socioeconomic Status

The NA population still faces a large socioeconomic gap as compared to non-Hispanic whites. Data suggests that NAs report lower levels of educational attainment with 80.2% of the population having graduated high school and only 14.7% of the population obtaining a bachelor's degree [38]. The NA population also reports a lower income level at $41,882 and an unemployment rate of 42.5% of able-bodied persons, according to 2017 U.S. Census Bureau data [39]. The highest poverty rate by race is found among the NA population [39]. Comparatively, more than one third of non-Hispanic whites obtained a bachelor's degree or higher, while the median household income for this population was found to be $65,145 [38,39]. One study also noted that AIs have a significantly higher risk than non-Hispanic whites for medical cost difficulties [1].

Access to Healthcare

Indian Health Services (IHS) is an agency within the Department of Health and Human Services that is responsible for providing healthcare to the NA population [40]. It delivers medical care to approximately 2.6 million AIs in 37 states nationwide with 28 acute-care, 50-bed hospitals in eight of those states [40,41]. The focus of IHS is to deliver primary and obstetric care to tribes in the western United States, and thus, have little to no resources for complex cases such as DFU and LEA [41]. In 2018, Congress set the IHS budget at $4.7 billion USD, a reduction of $59 million USD below fiscal year 2017 [42]. Servicing 2.6 million AIs, each person using IHS services is essentially allocated $1,807 USD [42].

Provider Bias

There is evidence of both healthcare provider racism and unconscious racial biases. Green, *et al.* found significant pro-White bias among internal medicine and emergency medicine residents, while James SA supported this finding, indicating a "pro-white" unconscious bias in physician's attitudes towards, and interactions with, patients [43,44]. In a survey assessing implicit and explicit racial bias by Emergency Department (ED) providers in care of NA children, it was discovered that many ED providers had an implicit preference for white children compared to those who identified as NA [45]. Indeed, racism and stigmatization are identified as being many American Indians' experiences in healthcare.

A study published in 2018 found that NA participants reported more frequent episodes of poor treatment and lower levels of treatment satisfaction with Western medicine [45]. Native American persons were the most likely racial group to report discrimination in health care, with discrimination being perceived by 7.1% of the AI alone group, 8.8% of those identifying as both NA and white (add of those), 5.6% of AAs, 4.3% of whites, and 2.6% of Asian Americans [45]. Another study indicated NA parents were 25 times more likely to perceive racial discrimination in the healthcare service for their child than white parents [46]. Racist encounters experienced by NA persons also leads to fear of utilizing conventional healthcare services [47]. Due to this, many NA may even forego care altogether to avoid anticipated racism [48]. Other bodies of literature support this claim, indicating certain minority groups are more likely to have negative perceptions of healthcare professionals and services [17]. For the NA population especially, the injustices committed by Western health systems precipitates mistrust, and such institutions are believed to contribute to poor health [48]. Additionally, having strong cultural ties leads NAs to seek physicians of their own ethnic background, but with only about 0.5% of all practicing US physicians, this population remains grossly underserved [48].

Patient Attitude Towards Western Medicine

Western healthcare institutions also do not consider spiritual facets of health, which may be perceived as a limitation of such medicine because the biological healthcare model is not "holistic" [49]. Thus, many NAs seek counsel and care from traditional healers, whose treatment plans include plant-based medicines, rituals and ceremonies in order to re-establish mental, spiritual, emotional, and physical balance of the patient [50]. Yet many physicians express disagreement with their patients using traditional Native medicines while under their care because they are unsure of what Native medicine or traditional Native healing entails, further widening the cultural divide between NA patient and doctor [51]. In fact, research indicates that sickness explanatory models that are discordant between healthcare providers and patients may reduce communication efficacy, adherence to treatment plan, and negatively impact health [52].

With regards to self-care behaviors in NAs with diabetes-such as daily glucose monitoring, daily foot checks, smoking status, physical activity, and daily fruit/vegetable consumption – a study using the Behavioral Risk Surveillance System (BRSS) data reported that NAs are more likely to engage in higher levels of diabetic self-care as compared to AAs, Hispanics, and whites [53]. While this data is self-reported, another source used objective data to establish lower rates of HbA1c control and adherence to oral medication-compliance in the NA population, but similar blood pressure and cholesterol outcomes compared to whites [54].

Discussion

With the NA population being genetically predisposed to developing diabetes and peripheral artery disease, lifestyle factors are of utmost importance in minimizing complications such as foot ulceration and major amputation. Enforcing dietary restrictions such as limiting carbohydrates and sugar, tobacco and alcohol use, as well as increasing fruit and vegetable consumption and physical activity should be encouraged. Perhaps working with a Nutritionist or Dietician may facilitate healthier habits, and considerations to access to care should be taken into account. As such, home healthcare and educator visits, or online modules to increase health literacy and maximize well-being may benefit this population as it faces significant transportation difficulties.

There is particularly a well-demonstrated link between tobacco use and development of PAD, which is strongly linked to DFU and LEA [55]. Several studies have indicated that the NA population is a robust user of tobacco products [34,56]. Additional literature has found that AIs/ANs with diabetes were found to smoke two to three times the rate of those that are current non-diabetic smokers [36]. Furthermore, NAs with diabetes that are current smokers were more likely to have glycosylated hemoglobin A1c levels at 8.0% or higher [36]. Having poor glycemic control likewise increases the complication rate, especially with macrovascular injuries, and reduces favorable outcomes [17]. Thus, it is imperative to help NAs with smoking cessation to prevent these adverse manifestations.

With many NAs living in low socioeconomic factors and having poor access to health care, these patients are at a greater risk for diabetes-related cardiovascular disease, including PAD. One study found a relationship between eight-year incidence of LEA in NAs with diabetes and risk by sex, educational attainment, renal function, and glycemic control [21]. Additional research by the CDC supports this data, stating prevalence of DM and its complications varied by educational and socioeconomic status, with those having lower educational and income levels at an increased risk [13]. It can be postulated that with many NAs living in poverty and lacking health insurance, affording medication such as insulin or metformin is simply unreasonable. This could in part explain the poor HbA1c control and medication compliance.

According to Richardson, *et al.* who used data from the 2007 Health Information National Trends Survey, people of lower educational backgrounds were less likely to seek health information [57]. The participants that reported lower income also indicated decreased confidence in their ability to obtain health information, and higher levels of mistrust in Western healthcare professionals than whites and those of higher income [57].With many NAs desiring care of culturally-competent healthcare professionals, there is a need for more physicians that identify as NA. Several medical schools are attempting to fill this void. But in 2017, a mere 100 NA students applied and of those 100, only 42 NAs were accepted into medical school [58].

More work needs to be done in reaching out to AI students and encouraging them to consider a career as a physician. For so many, medical school – and even a bachelor's degree-seems like an unattainable dream. With reservations rampant with substance and alcohol abuse, domestic violence, and poverty, many NA youth do not have the same opportunities nor support as those living off-reservations [59,60]. Several studies have indicated that NA youth face higher levels of substance use, alcohol abuse, and smoking as compared to their non-Native counterparts [60,61]. Likewise, AIs face a substantially higher rate of alcohol-attributable death than whites [61].

There are programs that seek to inspire AI youth to pursue Science, Technology, Engineering, and Math (STEM) fields. The National Science Foundation awards grants to educational institutions that have ongoing projects, and even recruits students from underrepresented groups, including the NA population. Yet more programs should target elementary school education to inspire interest and expose the youth to careers in STEM, and even more work needs to be done to attenuate drug and alcohol use in NA adolescents.

Despite existence of such facilities dedicated to NAs, access to healthcare remains a disparity for many NAs. Indian Health Services hospitals face an increase in the number of NAs using their services yet offer a narrow scope of services and even more limited access to specialists [41]. Due to funding constraints, referrals to outside specialists are not always approved, and preventative care services such as mammograms are often denied[46] [41]. As such, NAs often have difficulty getting high-quality, timely healthcare. Because their hospitals are older, acute-care facilities, IHS struggles to adequately treat complicated inpatient cases, uses outdated equipment, and a shortage of essential medications raises concerns about patient safety. Certainly, Center for Medicare Services (CMS) found IHS hospital staff to lack training and knowledge on emergency procedures and attributed three patient deaths in 2014 to staff's lack of proficiency and inability to identify problems [41].

Yet there are 13 states without IHS facilities, and those that do have IHS institutions experience issues as described above [40]. Aside from IHS facilities, the NA population is becoming increasingly more urban, with 71% of the population living in urban areas, according to the US Census[38]. But many NAs lack health insurance and cannot afford medical care outside of IHS services, so many do without treatments or seeing a healthcare provider [62]. Many AIs have not seen a medical professional in over one year, citing costs [62]. Those NAs that do live in rural areas or on reservations also face difficulties with accessing healthcare, particularly preventative and specialty care. Additionally, almost half of the NA population live more than 60 miles from care, thus it is a lengthy drive to access services. Tribal lands also feature inadequate transportation infrastructure, making it difficult for NAs living on the reservation to travel to hospitals, among other places. The inferior road conditions often delay emergency responders from providing timely assistance and jeopardizes the health, safety, and security of tribal members and those utilizing tribal roads.

Another attempt at encouraging health insurance coverage and access for American Indians was put forth by the Affordable Care Act (ACA), an expansion to Medicaid that was signed into law in 2010. This insurance plan was geared toward low-income families to ensure coverage and attainment of health services. In 2015, nearly 1.5 million AIs were enrolled in Medicaid, and healthcare-facilities that serve primarily Native populations received most of their reimbursements from Medicaid [63]. With medications to manage diabetes covered under ACA, this may also help control poor HbA1c and improve compliance with treatment plan. While this may be a step in the right direction, future studies would have to look at whether the ACA has helped curb diabetic complications such as ulcerations and LEAs in the NA population.

Healthcare providers' biases may be influencing medical decision-making, shaping physician behavior, and produce a difference in medical treatment of patients of various ethnic backgrounds. A body of literature has indicated that higher implicit bias was associated with disparities in treatment recommendations, expectations of healing, pain management, and empathy [64]. It may even contribute to the disparities observed in major LEA. As demonstrated above, the NA population is more likely to undergo primary LEA and less likely to have limb salvage. This may be in part due to perceived non-compliance with treatment plan.

Perceived discrimination may be affecting self-care practices in NAs with DFUs or even prevent them from seeking treatment. Some studies have indicated that NAs with diabetes remain below the national average for adherence to self-management recommendation in daily foot checks and diabetes self-care behaviors [4,6] From a psychological standpoint, feelings of anxiety, fear, and dread at being diagnosed with diabetes may even influence care-seeking and self-care behaviors [52]. Furthermore, NA elders perceived noncompliance with medical recommendations as socially desirable [52]. Thus, perhaps a more culturally-sensitive approach to medical care and education such as diabetes self-care classes may help to increase compliance and reduce complications.

Some medical experts have urged Western physicians to partner with traditional healers in order to best serve the NA patient. This may help reduce the anxiety and perceived discrimination and engage the patient more in their own care. Of note, some centers offer traditional food and even employ a traditional healer to accommodate its roughly 40% NA population[78] [65]. Future studies should look at compliance rates with cultural-appropriate treatment plan, and if it shows promising results, apply these practices to other hospitals that serve the NA populations.

In 1997, Congress established the Special Diabetes Program for Indians in response to the diabetes endemic that was hitting the NA population [66]. The $150 million USD grant allows for funding of 404 IHS, tribal, and urban health programs across the US to help prevent and treat diabetes [66]. A lifestyle intervention is a part of the program, enforcing such factors as healthy eating and physical activity [66]. To date, roughly 4,500 participants have completed follow-up assessments and demonstrated improvement in key diabetes risk factors [66]. The Native Diabetes Well Program by the CDC aims to honor the balance of cultural practices and western science in Indian Country to promote health and help prevent type 2 diabetes among NAs who are at risk [67]. It provides books for school-aged children about preventing DM while respecting traditional ways, educational and reference materials, and even a Traditional Foods Program that played a role in addressing food insecurity in NA communities [67]. These programs have also intervened and offered insight to Tribal schools as they developed their health and wellness policies. Longitudinal data will need to be collected in order to determine efficacy of these programs, and whether or not they are helping to curb incidence of DM in younger NAs.

Conclusion

The complications of diabetes, including foot ulcers and LEAs, are severe and costly to society. Compared to other groups, NAs experience a disparate rate of diabetes, DFUs, and LEAs. Factors leading to disparities in diabetes-related amputations in this population include personal, environmental, and healthcare level determinants. There is a pressing need to address the health disparities among the NA population, which is at-risk and often underserved.

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Conflicts of Interest

None.

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