Valley Fever Outcomes, Occurrences, & Occupational Risks in Vulnerable Populations in California & Arizona: A Systematically-Approached Review of Literature

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Abstract

Coccidioidomycosis, colloquially known as Valley Fever, is a fungal infection that is caused by the inhalation of naturally-occuring Coccidioides fungal spores. These spores are endemic to arid, dusty climates, which makes the southwestern United States a perfect breeding ground for this fungus. California and Arizona are the two states with the highest incidence rate of Valley Fever annually, but little is known about the risk factors associated with the high rates of infection in these particularly susceptible populations. A systematically-approached review of literature, which followed a framework in line with the 2020 PRISMA Framework, was conducted to discover potential relationships between sociodemographic, occupational, and health-related risk factors that could exacerbate the risk of disease in certain populations. Seven, peer-reviewed articles were chosen and critically appraised to determine their validity and relevance to the overarching research question. Results found that risk factors were not consistent between the two states. Articles found that there was evidence of misdiagnosis as a common negative health outcome and African American and male identify as social-racial factors that heightened risk in both Arizona and California. However, state-level differences resulted in the state of California having evidence of a relationship between workplace dust exposure and HIV/AIDS as risk factors for coccidioidomycosis hospitalization that was not seen in Arizona. External and internal limitations of the selected studies are potential causal agents that could have skewed the results. Further research is needed to determine the impact each of these factors have on the diverse populations of California and Arizona.

Keywords*:* valley fever; coccidioidomycosis; california; central valley; san joaquin valley; arizona; social determinants of health; farm laborers; construction; hispanic; african american; asian-american pacific islander.

Valley Fever Outcomes, Occurrences, & Occupational Risks in Vulnerable Populations in California and Arizona: A Systematically-Approached Review of Literature

Valley Fever, also known as *Coccidioidomycosis*, is a fungal infection brought about by inhalation of *Coccidioides* fungal spores (which naturally occurring in the soil of some regions and travel through the air as microscopic particles or dust matter when the soil is agitated) (CDPH, 2024). Valley Fever is endemic to the Southwestern United States, with most cases occurring in the states of California and Arizona (CDPH, 2024). In 2022 alone, there were 17,612 reported to the Center for Disease Control and Prevention (CDC), with 7,459 cases from California and 9515 from Arizona, respectively. To put these statistics into perspective, of the 17,612 Valley Fever cases reported to the CDC in the year 2022, only 284 cases were reported in the other endemic U.S. states (Utah, Nevada, & New Mexico), and the remaining 992 cases were reported from all non-endemic states combined. (CDC, 2024).

It is evident that there is a clear need for efforts to combat the high incidence of Valley Fever in California and Arizona, however, significant barriers make recognizing and creating targeted interventions for those affected challenging. In order to be diagnosed with Valley Fever, an individual must present with symptoms that meet the disease's case definition. Case definition symptoms of Valley Fever include fatigue, coughing spells, shortness of breath, body aches, or an erythematous rash (CDC, 2024).

However, despite having a clearly-defined case definition and being a disease that is closely monitored by the CDC's National Notifiable Disease Surveillance System, the incidence of Valley Fever is grossly underreported. According to work done by Grizzle et al. (2020), it was found that about 60% of cases of Valley Fever are asymptomatic, and of the ones that are symptomatic, the clinical presentation was hard to differentiate from other common respiratory

illnesses. Similarly, Sondermeyer et al. (2013) found that most cases of Valley Fever in California are asymptomatic, and only approximately 40% of patients will develop symptoms (which varied in severity from mild flu-like symptoms to chronic meningitis) after infection (Sondermeyer et al., 2013). A lack of conclusive evidence of infection makes treating and testing patients for infection extremely difficult, leading many healthcare providers to miss or misdiagnose patients.

Unlike many other commonplace pathogens that infect individuals indiscriminately, the *Coccidioides* fungus isn't so kind. Social, political, and environmental climates inadvertently place certain populations at higher risk for development of this debilitating condition. By examining the variables and risk factors associated with coccidioidomycosis infection and how having a heightened risk affects the health outcomes of those infected, this review of literature seeks to raise questions about how race, socioeconomic status, occupation, individual health experiences, and other related social-political factors predispose certain individuals to infection and a potentially lifelong burden of disease.

Methods

Employment of the PRISMA Framework

This systematically-approached review of literature follows methodology that is based on the 2020 PRISMA framework for systematic reviews. In accordance with the guidelines set by the PRISMA Executive, this review of literature compiled sources through a comprehensive search of UC Davis' library databases. These research articles were then pooled from their respective databases, screened by the researcher to exclude irrelevant articles though a review of their abstracts, and read in their entirety to determine whether they were eligible for inclusion in

the final review (PRISMA Statement, 2024). Of the articles read, seven peer-reviewed articles met the criteria needed and were included in the final review.

Inclusion and Exclusion Criteria

While taking extra caution to be mindful of prior work done on the subject when searching for articles, a large-scale, an exclusionary search was conducted. Search criteria for articles was limited to sources published within 2013 or after, and focused specifically on Valley Fever in either California, Arizona, or both regions. Boolean operators were employed at this stage to assist the database in selecting articles that met the aforementioned criteria.

Foreground, scholarly peer-reviewed sources were drawn from the Scopus, PubMed, Cinahl databases, whereas other background sources were pooled from public-domain government websites (ex. CDPH, CDC, etc.). To further refine the search in PubMed and Cinahl, the MeSH terms, “”California/epidemiology” and “Epidemiology+” respectively, were used. The Scopus database was used for “snowballing,” which allowed researchers to find other related sources to be pulled from the Cinahl and PubMed databases using the above keywords, MeSH terms, and the inclusion and exclusion criteria.

Critical Appraisal of Selected Literature

The CASP (Critical Appraisal Skills Programme) critical appraisal guidelines were used to determine the validity and strength of the selected articles. These guidelines were used to assess seven articles with varying methodologies, which included four cross sectional studies, one case-control studies, one cohort study, and a case study article. The critical appraisal process conducted accounted for differences in data collection, and varying amounts of both quantitative and qualitative data present in each article, only articles that demonstrated satisfactory conduct in their respective category (according to the CASP guidelines) were deemed fit for inclusion.

Results

Sociodemographic and Economic Factors Associated with A Heightened Risk for Infection

Complex social constructs (race, class, and gender), more commonly known as the social determinants of health, contribute significantly to the overall health status and risk associated with coccidioidomycosis infection in particular populations. Sondermeyer et al. (2013) and Kupferwasser & Miller (2020) both found significant associations between race, class, and gender in the determination of coccidioidomycosis hospitalization.

To further explore the relationship between sociodemographic factors and Valley fever infection, Sondermeyer et al. performed a cross-sectional study that focused exclusively on coccidioidomycosis hospitalizations in California residents through analysis of state coccidioidomycosis hospitalization data from the Office of Statewide Health Development and Planning's 2000-2011 California Patient Discharge Dataset. The data was further broken down to account for primary and secondary diagnoses of coccidioidomycosis, and patient data was matched with Social Security numbers, date of birth, and demographic data to draw important conclusions about demographics, age, and socioeconomic status. Results found that more than 50% of the 15,747 patients who were initially hospitalized for coccidioidomycosis were male-identifying (a rate 2.48 higher than that for women). The research team also found that African American had the highest yearly incidence of hospitalization and Asian/Pacific Islanders the lowest incidence in the year 2011 (Sondermeyer et al., 2013).

Contrarily, a similar cross-sectional study on the sociodemographic profile of patients hospitalized in the states of California and Arizona found differing results. Using the HCUP database for hospital intake data, Kupferwasser & Miller also examined the prevalence of sociodemographic factors in the incidence of Valley Fever hospitalization. The study looked at

data from the years 2005-2011, and found that of the 23,758 cases of Valley Fever between both states, African Americans and Asian American/Pacific Islander had the highest incidence rates for coccidioidomycosis in California and Arizona across all years observed. The hospitalization rate for the HCUP dataset was greatest for African American, Hispanic, Native American/Alaskan Native, and those who reported "other" for race and ethnicity, and being female was indicated with a lessened risk for hospitalization of coccidioidomycosis (Kupferwasser & Miller, 2020).

Differences in both race/ethnicity and genders were not explicitly discussed in the studies above, but potential explanations for these differences include variance in state demographics, social and political barriers to access, and historical misrepresentation and ostracization of particular race/ethnicities.

Occupational Hazards as Risk Factors for Coccidioidomycosis Infection

Occupations and the environments individuals thrive and live in significantly impact their risk for inhalation of Coccidioides spores. There is a strong relationship between levels of occupational dust exposure and the incidence of coccidioidomycosis. A case-control study by McCurdy et al. (2020) on Hispanic farm laborers working in endemic Kern county found evidence that the types of crops an individual worked with affected their individual rate of infection. McCurdy et al. were able to survey 1,803 Hispanic farm workers who had confirmed positive serological tests, and asked them questions about the dust exposures they encountered at work and what types of crops they harvested.

Results found that the risk for contracting Valley Fever was significantly increased for Hispanic farm workers working with bulb and root vegetables (a three-fold higher risk compared

to controls), and that increases in self-reported levels of dust exposure at work correlated with an increased incidence of Valley Fever.

Similarly, Nicas' (2018) case study on an oil field worker in CA also reported similar findings. Nicas' case study focused on following the experiences of an oil-field worker, "Mr. A," and his experience with contracting Valley Fever, being misdiagnosed, and his development of Valley-Fever related pneumonia as a result of his 33 days working at the McKittrick Oil Field in Kern County, CA.

The study ultimately found that only after working 11 days on the oil field, Mr. A developed Valley Fever. In order to understand what workplace-related factors could have contributed to the Mr. A's rapid development of Valley Fever, Mr. A was asked about his working conditions. In response, Mr. A stated that his provided skid steer had an open cab, a lack of air conditioning, and a faulty excavator. Because of this, he was forced to leave the door slightly ajar, which allowed lots of dust to accumulate in the cab and settle on the seat next to him. The small space in the cab, combined with a potential lack of HEPA-air filters, could have exacerbated Mr. A's risk of exposure (Nicas, 2018).

On the contrary, Blair et al. (2014)'s longitudinal, cohort study found a heightened risk of long-term Valley Fever incidence in areas further away from places with active construction and soil agitation. Blair et al.'s cohort study examined incidence rates of Valley Fever in employees working at or near an Arizona research campus that was under construction. 176 employees from Campus A, which was situated beside an active construction site, and 140 employees from Campus B, which was a sister campus located 13 miles away from the construction site. Employees were asked to provide a baseline serological sample and individuals with a

seropositive sample were asked to provide another sample a year later for comparison (Blair et al., 2014).

Examination of employees at two campuses (A & B), with A being situated beside an active construction site and B being located 13 miles away, found that while 20 of the 176 employees at Campus A (11.4%) showed prior, hidden coccidioidal infection at the start of the study (which occurred a year after construction was completed) and 19 of 140 (13.6%) exhibiting signs of infection at Campus B (Blair et al., 2014). A year after immunological testing, only 2.5% of employees at Campus A had evidence of a new coccidioidomycosis infection and a staggering 8.9% of employees at Campus B had evidence of a new infection.

These three studies evidence the relationship between workplace exposure and the incidence of Valley Fever. The two California studies (Nicas (2018) and McCurdy et al. (2020)) find a significant, increased relationship between the development of coccidioidomycosis in laborers working closely with soil. However, Blair et al. (2014) found a negative relationship, with rates of Valley Fever being higher in areas further from active construction zones. There was no discussion on whether or not these differences could be explained by state level differences (ex. differences in infrastructure, climate, or soil composition).

Misdiagnosis and Other Related Adverse Health Outcomes Associated with Prolonged Valley Fever Infection

Misdiagnosis and related adverse health outcomes that arose from prolonged infection were also examined to determine the long-term effects that a Valley Fever diagnosis (or lack thereof) had on an individual's physical and mental wellbeing. A cross-sectional study by Donovan et al. (2019) examined the effects of misdiagnosis on Arizona patients through retrospective analysis of 815 patient health records from Banner University Medical Center in

Tucson, AZ over a 2.7 year period. Of those 815, 276 had coccidioidomycosis related reasons for visiting this hospital. This study focused on examining the cost burden and average length of times patients had to wait to be properly diagnosed through statistical analysis (Donovan et al., 2019).

Results found that there was a positive correlation between cost burden on the healthcare system and the length of delay in diagnosis of a coccidioidomycosis infection in Arizona. Of the 276 coccidioidomycosis patients examined, 246 experienced a delay in diagnosis that was greater than 1 day, resulting in the accrual of $589,053 in costs (which was 82% of the $718,401 spent by all patients combined) (Donovan et al., 2019). The median length of delay was anywhere from 17 to 54 days, with approximately 43% of patients experiencing a delay lasting longer than a month (Donovan et al., 2019).

Similarly, Nicas' (2018) case study of an individual suffering from an undiagnosed case of coccidioidomycosis reveals similar disturbing trends. Mr. A, the individual followed in the case study, went to the emergency department after working 11 days at the McKittrick Oil Field in Kern County, CA with primary complaints of dizziness, nausea, and other common URI (upper respiratory infection) symptoms. He received a chest x-ray that did not show any acute respiratory disease, was given medication to alleviate his symptoms, and cautioned to take time off from work. It was only after leaving California (22 days after his ER visit) and returning home that he was diagnosed with coccidioidomycosis-related pneumonia.

Additionally, hospitalization was a common adverse outcome observed in both states. Studies conducted by Sondermeyer et al. (2013) and Kupferwasser & Miller (2020) found that certain comorbidities and hospital intake experiences contribute to the long-term health status of patients. In a cross-sectional study conducted by Sondermeyer et al., it was found that of the

25,217 coccidiomycosis-associated hospitalizations found in the Office of Statewide Health Planning and Development's CA Patient Discharge Data Set, only 15,747 (approximately 62%) of patients were initially hospitalized for coccidioidomycosis and that the remaining 38% were subsequently hospitalized, meaning they were initially admitted for another condition and had their reason for hospitalization changed to coccidioidomycosis post-hospitalization (Sondermeyer et al., 2013). Similarly, Kupferwasser & Miller found that of the 23,758 hospitalizations in the states of California and Arizona, 72% of patients were initially diagnosed with coccidioidomycosis, and the remaining 28% being given a subsequent diagnosis (Kupferwasser & Miller, 2020).

Sondermeyer et al. (2013) also found that individuals with select concurrent conditions were more likely to be hospitalized with Valley Fever in California. It was found that of the 15,747 patients hospitalized with an initial coccidioidomycosis infection, approximately 33% had comorbidities, with HIV/AIDS and diabetes being disproportionately overrepresented in this group. About 2.8% of individuals had an HIV/AIDS diagnosis as well (which is high compared to the approximately 0.3% prevalence in the state of California). In addition to this, 22% had a concurrent diagnosis of diabetes, which is significantly higher than the age-adjusted 7.7% prevalence in CA's population (Sondermeyer et al., 2013). On the contrary, Kupferwasser & Miller (2020) found that in their HCUP data for both the states of California and Arizona, individuals with an AIDS diagnosis were at less risk for hospitalization, and that risk for coccidioidomycosis hospitalization was increased in those with diabetes and COPD (Kupferwasser & Miller, 2020).

Discussion

The studies examined in this review of literature showed mixed results regarding the impacts that certain sociodemographic, economic, occupational, individual health experience, and other social-political factors have on the health outcomes and the increased incidence of coccidioidomycosis in vulnerable populations. Results were further confounded by overarching, contradictory differences in data collected in California and Arizona. Specifically, Kupferwasser & Miller's (2020) study about hospitalization from the years 2005-2011 in CA and AZ found that AAPI individuals had increased incidence of coccidioidomycosis, but this was heightened risk of development was not indicated in the data collected by Kupferwasser & Miller. Results ultimately found that AAPIs did not have higher rates of hospitalization compared to other minority groups and that being African American and male was indicated with higher risk in both the states of California and Arizona (Kupferwasser & Miller, 2020) (Sondermeyer et al., 2013).

Reasons for this disparity could be attributed to differences in state populations, as well as race-related health outcomes and levels of access to care. However, limitations to both studies make drawing this conclusion difficult. While both Sondermeyer et al. and Kupferwasser and Miller examine California residents in their studies using their respective databases, there is no data collected that focused on Arizona specifically. In addition to this external limitation, Kupferwasser & Miller and Sondermeyer et al. acknowledge that their usage of their respective database for their data means that government-affiliated hospitals (ex. Indian Health Services, VA, etc.) were not included in their studies. Lack of data on these individuals could mean that incidence rates and the collected sociodemographic data is not truly representative of the diverse populations of either state.

Sondermeyer et al. (2013) continue their discussion of risks by further extrapolating that the heightened risks for African American/Hispanic and male individuals studied was justified due to the high levels of dust exposure in predominantly male-dominated jobs (ex. farm labor and construction), and the known risk that African Americans and Hispanics are at a greater risk for disseminated disease (which means that the infection has spread from the initial infection site and began to attack other organ systems) (Sondermeyer et al., 2013). These factors are consistent with the findings from both Nicas (2018) and McCurdy et al. (2020)'s case study and case-control study, respectively. Nicas found that Mr. A, a male working in construction on an oil field in the endemic San Joaquin Valley in California, developed Valley Fever due to the high levels of dust he encountered at his work (Nicas, 2018). Likewise, McCurdy et al. found that Hispanic farm laborers who self-reported encountering more dust at work had a higher risk of Valley Fever, and those who worked more closely with crops near the ground were 3x more likely to develop Valley Fever (McCurdy et al., 2020). However, Blair et al. did not find a significant association between exposure to dust in active areas of construction in Arizona, and actually found that those who were located slightly further, actually showed a consistently higher incidence rate (Blair et al., 2014)

Consideration of these articles determined that while there is a possible association between race, occupational dust exposure, and development of Valley Fever in the state of California, this may not be the case in Arizona. However, the small, limited sample size used in Blair et. al's AZ study, Nica's case study, and McCurdy et al.'s case-control study, indicate that more research is needed to what role race and occupation play in the development of this complex condition.

In addition to the above findings on hospitalization, occupation, and sociodemographic factors, Donovan et. al (2019), Nicas (2018), Kupferwasser & Miller (2020), and Sondermeyer et al. (2013) found that while misdiagnosis is a possible negative health outcome for those with a Valley Fever infection, comorbidity factors related to hospitalization are not as clearly defined.

Both Nicas and Donovan et al. found that misdiagnosis significantly reduced the health of those infected, but both external and internal limitations and a lack of supplemental data within these studies make it difficult to find a clear correlation between the long-term effects and misdiagnosis rates. Without more generalizable data for Arizona (ex. expanded studies with a larger sample size that would be more representative of the state's diverse population) and more literature on the long-term effects (economic and physical) that misdiagnosis has on California patients, results remain inconclusive.

In similar fashion, Kupferwasser & Miller (2020) and Sondermeyer et al. (2013) also came to an inconclusive conclusion regarding the correlation between comorbidities and rates of hospitalization. While both studies found that co-infection with diabetes was indicated with a heightened risk for coccidioidomycosis hospitalization, there was disagreement on whether or not HIV/AIDS had similar effects (Kupferwasser & Miller, 2020) (Sondermeyer et al., 2013).

These differences in results could be attributed to limitations within these studies as well as differences in disease prevalence between the two states. The state of California has a higher prevalence of HIV/AIDS than the state of Arizona (CDC, 2016). This difference in prevalence could explain why Sondermeyer et al. found HIV/AIDS to be a greater contributor to coccidioidomycosis hospitalization than Kupferwasser & Miller.

Conclusion

Coccidioidomycosis infection is a complex, multifactorial issue that affects the health and longevity of individuals living in California and Arizona. Two of the seven articles indicated that there may be a strong relationship between misdiagnosis and negative health outcomes for individuals residing in both the states of California and Arizona. However, the same cannot be said for the other factors studied. Most of the articles studied were able to find a relationship in their respective state, but that data was not consistent between Arizona and California. Examples of this include another pair of the seven articles comparing hospitalization demographics found inconclusive evidence regarding the rate of infection of AAPI individuals, or how workplace dust exposure was found to be a significant indicator of Valley Fever infection in CA but not in Arizona. State-level differences and external and internal limitations within the studies chosen for review make comparison and definitive correlations difficult to make. Ultimately, this review of literature was not able to find concrete evidence of risk factors that affect vulnerable groups' rate of infection. Further research, with a smaller scope that focuses on and embraces the diverse populations and demographics represented in each state, is needed to come to a decisive conclusion.

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