A Comprehensive Systematic Literature Review of Merkel Cell Carcinoma Epidemiology in the United States

EPH205

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INTRODUCTION

- Merkel cell carcinoma (MCC) is a rare, aggressive neuroendocrine carcinoma, associated with a high risk of local recurrence and distant metastases[1]
- It primarily occurs on sun-exposed skin, with a higher prevalence among elderly White men. The head and neck region is most commonly involved, followed by the upper and lower extremities and the trunk[1,2]
- Despite advancements in treatments like immunotherapy, MCC remains associated with poor prognosis, underscoring the need to understand region-specific epidemiological trends for optimizing treatment strategies and improving patient outcomes

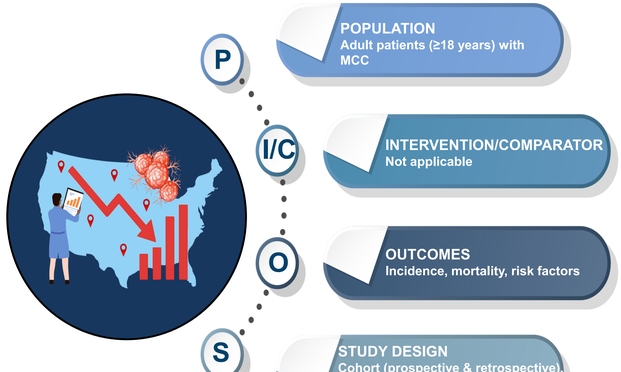
OBJECTIVE

- The current systematic literature review (SLR) aims to understand the epidemiology of MCC across the United States (US)

METHODS

- This review followed the standard methodology for conducting an SLR as per guidelines provided by the National Institute for Health and Care Excellence (NICE)[3]
- Electronic databases such as EMBASE® and MEDLINE® were searched to identify relevant MCC studies reporting epidemiological data. US-specific, English-language articles published within the last 10 years were included
- The SLR encompassed a comprehensive range of study designs, including prospective and retrospective observational studies, cross-sectional analysis, and case-control studies, to gather epidemiological data pertaining to MCC
- The standard Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) compliant two independent review and quality control process was followed during data collection
- The prespecified eligibility criteria are presented in **Figure 1**

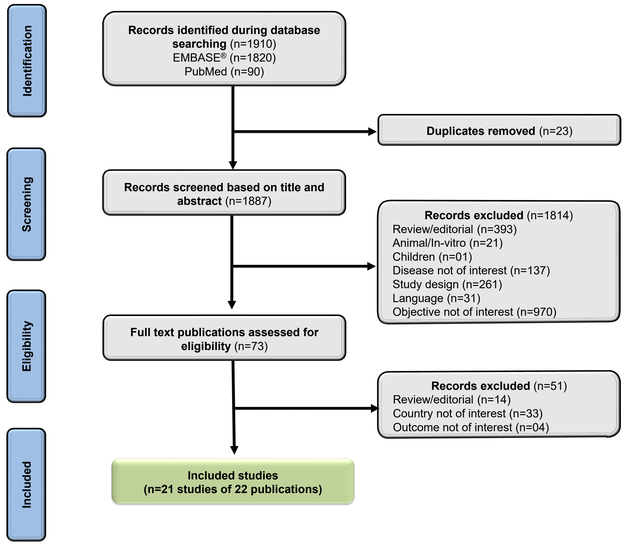
Figure 1: Eligibility criteria for selection of evidence



RESULTS

- A PRISMA diagram for the screening process is presented in **Figure 2**
- A total of 21 studies were included, comprising 15 journal articles and six conference abstracts, providing US-specific epidemiological data on MCC

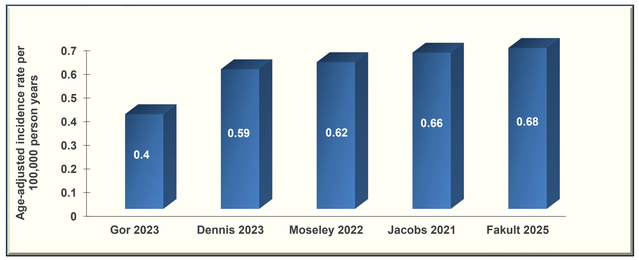
Figure 2: PRISMA diagram for the screening process



Incidence

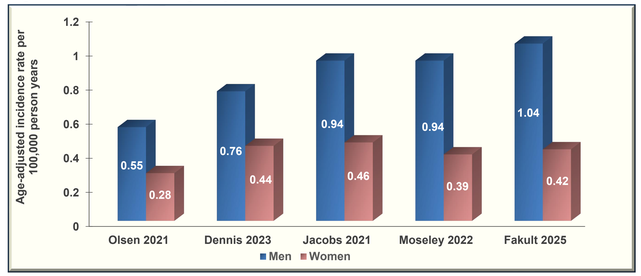
- As per the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) database, the age-adjusted incidence rate (AIR) of MCC ranged from 0.40 per 100,000 person-years (PY) (2004-2015) to 0.68 per 100,000 PY (2013-2021) **(Figure 3)**

Figure 3: Age-adjusted incidence rate of MCC



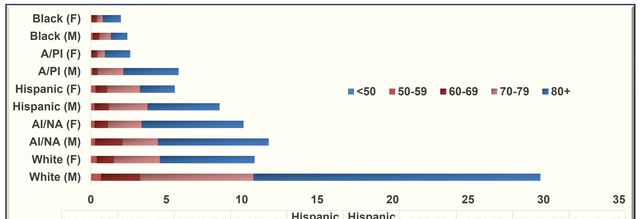
- Incidence rates were consistently higher among men, with a two-fold increase in AIR from 0.55 to 1.04 per 100,000 PY between 1997-2021, whereas a modest increase was observed among women from 0.28 to 0.46 per 100,000 PY between 1997-2016 **(Figure 4)**

Figure 4: Gender-based age-adjusted incidence rate of MCC



- The AIR across all age groups was consistently higher in men compared to women among Whites (1.36 vs 0.53), followed by American Indian/Native Alaskan (AI/NA; 0.55 vs 0.45), Hispanic (0.41 vs 0.30), Asian/Pacific Islander (A/PI; 0.26 vs 0.12), and Blacks (0.14 vs 0.10)[1] **(Figure 5)**

Figure 5: Age-adjusted incidence rate of MCC by sex, race and age subgroup

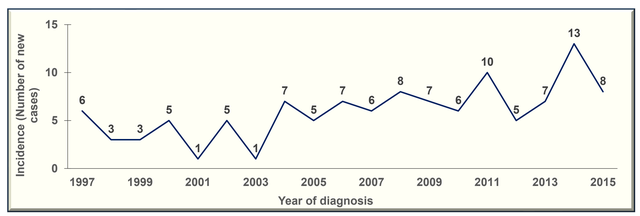


	White (M)	White (F)	AI/NA (M)	AI/NA (F)	Hispanic (M)	Hispanic (F)	A/PI (M)	A/PI (F)	Black (M)	Black (F)
<50	0.03	0.02	0	0	0.01	0.01	0	0	0.02	0.01
50-59	0.66	0.37	0.28	0.26	0.24	0.31	0.13	0.07	0.13	0.05
60-69	2.6	1.15	1.84	0.88	0.96	0.78	0.35	0.36	0.42	0.35
70-79	7.49	3.03	2.32	2.23	2.55	2.15	1.68	0.51	0.76	0.38
80+	19	6.27	7.34	6.75	4.76	2.31	3.65	1.67	1.08	1.19

Age-adjusted incidence rate per 100,000 person years

- As per SEER-22 database, the AIR among individuals of American Indian/Alaska Native descent was higher (0.40 per 100,000 PY) compared with Non-American Indian/Alaska Native individuals (0.325 per 100,000 PY)[4]
- MCC diagnosis increased over time (1997-2015) among 113 cases from a retrospective chart review, with 2.3 times higher number of cases observed in the last three years compared to the first three years[5] **(Figure 6)**

Figure 6: Number of MCC diagnoses per year from 1997 to 2015

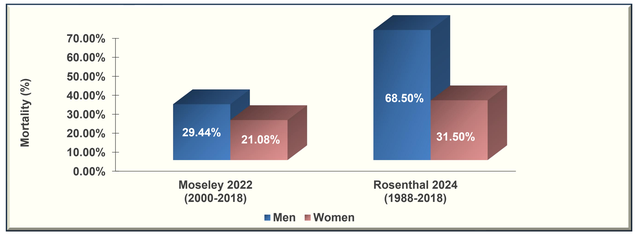


- The overall age- and sex-adjusted incidence of MCC during 1976-2011 was 0.35 per 100,000 PY with higher incidence among men than women (0.69 and 0.10 per 100,000 PY) respectively[6]

Mortality

- Overall mortality increased steadily from 0.03 to 0.43 per 100,000 PY between 1986 and 2011[7]
- Across 2000-2018 study period, MCC mortality rates were higher in men compared to women (29.44% vs 21.08%). A similar pattern was observed over the longer period (68.50% vs 31.50%) from 1988 to 2018 **(Figure 7)**

Figure 7: MCC mortality based on gender



- Overall and disease-specific mortality rises with age >65 years (Hazard ratio; HR: 3.82 and 2.46), tumor size>40 mm (HR: 2.26 and 2.90), and distant metastasis (HR: 3.03 and 7.44) respectively[8]

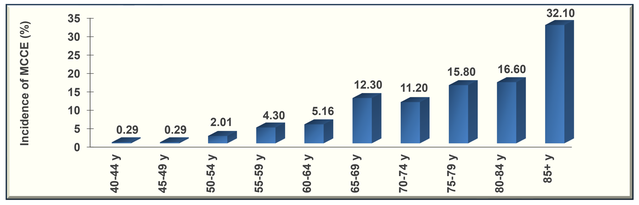
Risk factors

- The risk of MCC was significantly higher in men than in women (p<0.001), individuals aged ≥35 years compared to those <35 years (p<0.001), organ transplant recipients (p<0.001), and ultraviolet radiation exposure (p=0.005). Further, White patients have 7.4 times higher risk compared to Black patients[1,9]

Incidence of MCC of eyelid (MCCE)

- MCCE comprised 349 identified cases, accounting for 2% of all MCC cases reported between 2000-2019. Females were significantly more affected than males (56.60% vs 44.40%, p<0.05), and the majority of cases occurred in White patients (90.80%) compared to Black patients (2.90%)[10]
- Incidence increased significantly with advancing age, with the majority of patients being 85 years of age or older (p<0.05) [10] **(Figure 8)**

Figure 8: Incidence of MCCE based on age



LIMITATIONS

- No studies were identified that reported prevalence data, limiting the ability to estimate the overall impact of disease in the population
- Another limitation is the potential under-reporting of MCC cases in cancer registries, which may affect the accuracy of incidence estimates

CONCLUSIONS

- The incidence of MCC shows a clear and rising trend across the US over recent decades, with notable gender-based variations reflecting its growing epidemiological significance
- These findings underscore the growing burden of MCC, the need for enhanced awareness, and the importance of early detection to inform healthcare planning and targeted interventions

References

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Abbreviations: A/PI: Asian/Pacific Islander; AI/NA: American Indian/Native Alaskan; AIR: Age-adjusted Incidence rate; EMBASE: Excerpta Medica Database; F: Female; HR: Hazard ratio; M: Male; MCC: Merkel cell carcinoma; MCCE: MCC of eyelid; NICE: National Institute for Health and Care Excellence; PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-analyses; PY: Person Years; SEER: Surveillance, Epidemiology, and End Results; SLR: Systematic Literature Review; US: United States

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