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Pregnancy after a melanoma diagnosis in women in the United States



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ABSTRACT

Background: Melanoma is the third most common cancer in women aged 18–39 years. Medical literature recommends that women wait for at least 2 years before becoming pregnant, yet few studies have examined pregnancy after melanoma. Our aims were to investigate the pregnancy rate after a melanoma diagnosis and the relationship between melanoma treatment and subsequent pregnancy.

Methods: We studied women with a melanoma diagnosis in the Truven Health MarketScan database. Women with a melanoma diagnosis were matched 1:1 to women with no melanoma diagnosis to compare pregnancy rates between groups. For women with melanoma, Cox models were fitted for rates of pregnancy overall, pregnancy if postsurgical treatment was received, and for treatment after pregnancy.

Results: The sample included 11,801 women aged 18–40 years with melanoma, who were not pregnant on the index date. These women had a higher rate of pregnancy within 2 years compared to matched controls (15.8% versus 13.6%, $P < 0.001$). For 0–9 months after diagnosis, women who received postsurgical treatment had a 74% lower probability of becoming pregnant (hazard ratio = 0.26, $P = 0.003$). Rates of treatment received after pregnancy were not significantly different (hazard ratio = 0.68, $P = 0.23$).

Conclusions: Our study is the largest review of postmelanoma pregnancy in the United States. After a melanoma diagnosis, women had a slightly higher rate of pregnancy than matched controls, indicating that women are not delaying pregnancy. However, women who received advanced treatment for melanoma had a lower rate of pregnancy than untreated women. Women who became pregnant after a melanoma diagnosis did not have an increased risk of requiring subsequent treatment for melanoma.

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Introduction

The incidence of melanoma in women aged 18-39 years has been increasing annually, with melanoma being the third most common cancer in this age group.¹ Most cases of melanoma in the age group 0-39 years occur in women, unlike the ratio in older patient populations.² Melanoma thus affects women in their prime childbearing years and in steadily increasing numbers. Traditionally, patients who are pregnant at the time of diagnosis of melanoma have been thought to have a poor prognosis, and it is believed that subsequent pregnancy after treatment for melanoma might increase the risk of recurrence.^{3,4} More recent literature finds that women who are pregnant at the time of diagnosis of melanoma have the same prognosis as other patients of the same stage. What is unclear and difficult to study is the relationship between melanoma and subsequent pregnancy rates, and pregnancy on melanoma outcomes. Very little data exist to guide women and physicians as to the safety of pregnancy after a diagnosis of melanoma. As a result, there are no formal guidelines for physicians who wish to counsel their patients regarding pregnancy after melanoma, and it is unknown whether women receive any counseling at all.

For this study, our primary aim was to determine the incidence of pregnancy after a diagnosis of melanoma compared to a matched comparison group without melanoma. Our hypothesis was that women diagnosed with melanoma would have a lower rate of pregnancy than women without melanoma, as many physicians recommend waiting for at least 2 years after diagnosis to become pregnant.⁵ We also sought to examine women with more advanced or recurrent melanoma, as indicated by receiving additional surgery, systemic or radiation therapy, referred to collectively as postsurgical treatment in this study. Our secondary aims were to examine the relationship between treatment and pregnancy among the patients who had a melanoma diagnosis. Our hypotheses were that women who had more advanced disease would be less likely to become pregnant but that women who become pregnant after a diagnosis of melanoma would not require additional treatment compared to nonpregnant women.

Materials and methods

Patient cohort

We performed a retrospective cohort study of women with a diagnosis of melanoma during their childbearing years using the Truven Health MarketScan database.⁶ This study was deemed exempt from IRB review. This database includes patients enrolled in commercial health plans and captures claims on more than 50 million covered lives across the United States. The database includes all inpatient, outpatient, and office claims. From the MarketScan database in the years 2005-2011, we selected all inpatient and outpatient claims with a diagnosis of active melanoma or history of melanoma for female patients aged 18-40 years. Diagnoses were determined using International Classification of Diseases, 9th

revision, Clinical Modification (ICD-9) codes for active melanoma (172.X) and for history of melanoma (V10.82). Patients often had multiple claims with diagnosis codes for melanoma. For this analysis, we used the earliest claim (by date). We refer to this as the index date. The cohort was limited to only those women who were continuously enrolled in an insurance plan from 3 months (90 days) before the index date to 2 years (730 days) after the index date.

We matched each patient with a diagnosis of melanoma to a patient in the MarketScan database who did not have a melanoma claim at any time point. For patients without a melanoma claim, we randomly assigned a pseudo-index date from the set of all dates in which the patient was covered by an insurance plan. The pseudo-index date represents the date in which a patient without a melanoma diagnosis could have had a claim for melanoma. We calculated age, enrollment time in an insurance plan, state of residence, and pregnancy status conditional on the pseudo-index date. A total of 2,924,326 female patients with no melanoma claims (at any time) met the same criteria as the melanoma cohort based on the pseudo-index date. These patients formed the set of possible matches for our melanoma patients. We matched patients on the basis of the following criteria: year of index date (pseudo-index date), age at index date (pseudo-index date), state of residence, and pregnancy status within 90 days before index date (pseudo-index date). We selected state of residence as a surrogate for other factors including risk of melanoma and rates of live birth.^{7,8} A greedy matching scheme⁹ was used to obtain 1:1 matches. All matches were exact with three exceptions that occurred in small population states. For these exceptions, age (± 1 year) and year of index date (± 1 year) were allowed to differ.

Pregnancy and treatment status were determined for all patients using the ICD-9 diagnosis codes, ICD-9 procedure codes, current procedural terminology, and revenue center codes from all inpatient and outpatient claims (Table). Treatments included systemic therapy, radiation therapy, surgery (metastasectomy or lymphadenectomy), and biopsy for metastases.

Statistical analysis

For the primary aim of comparing rates of pregnancy within 2 years of diagnosis between melanoma patients and the matched comparison group, we used conditional logistic regression. For patients who were not pregnant at the index date, we investigated the rates at which patients became pregnant over time in each group using a survival analysis. The outcome was defined as the number of days from the index date to the date of first claim that indicated pregnancy. Patients who were never pregnant at 2 years after the index date were censored at that time point. The method of Kaplan and Meier¹⁰ was used to estimate cumulative incidence curves of pregnancy for each study group.

For the secondary aim of examining whether postsurgical treatment was related to pregnancy among patients diagnosed with melanoma, we used techniques from survival analysis. Treatment was (typically) unknown at the index date. Thus, we used a landmark analysis such that at

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