

Variation in immune function in relation to sun exposure and vitamin D

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Abstract. Although much is known about the relationship between UVR, vitamin D status and immune function, it is not yet understood whether immune markers vary with season as a result of seasonal changes in UVR and vitamin D levels. The purpose of this project was to determine if, and to what extent antibodies to common viruses vary seasonally, and whether UVR dose and vitamin D status are contributing factors to this pattern.

Introduction

Humans evolved at low latitudes under high levels of ultraviolet radiation (UVR). From their light-skinned forebears, they are thought to have developed dark skin pigmentation to protect against the harsh sunlight, particularly the damaging effects of degradation of skin folate (Jablonski and Chaplin 2000). Migration to higher latitude areas of lower ambient UVR are thought to have caused selection for lighter skin colour, to ensure sufficient vitamin D could be made from the weaker and seasonal sunlight. During evolution, there was a close and ongoing relationship with injury and infection – it is thought that vitamin D and exposure to UVR caused modulation of immune function, to ensure an adequate, but not overzealous reaction to pathogenic threats (Hart and Gorman 2013).

In modern times, the close link between evolutionary adaptation and location has been lost – fair skinned people of European origin inhabit a high ambient UVR environment such as Australia and suffer high rates of skin cancer (AIHW 2012), having lost the protection of darker skin pigmentation. Dark-skinned populations migrating to higher latitude locations suffer vitamin D deficiency (Skull *et al.* 2003). And in both, the careful balance between “adequate but not overzealous” response of the immune system is threatened.

The Seasonal D Immune Function (SDIF) Study aimed to better understand seasonal variation in immune function and whether this occurs in parallel and as a result of seasonal fluctuation in exposure to UVR and/or vitamin D status. This study will have important implications for broadening our understanding of seasonal infection epidemiology and for future research into the effects of vitamin D status and UVR on immune function.

Methods

A volunteer sample of 58 participants was recruited from the SeasonalD study. Participant data were collected between October 2012 and July 2013. Data collected included body measurements, questionnaires, and UVR exposure by seven day sun diary and ambient UVR. Blood samples for serum 25(OH)D concentration and antibodies to common viruses were also taken. Data were analysed using regression and repeated measures analysis.

Results

Mean 25(OH)D levels, and median UVR dose, EBNA IgG, EBV VCA IgG and VZV IgG levels were plotted according to the month of collection (Figure 1). 25(OH)D levels and UVR dose (not clothing adjusted) varied by month of the year. There was no evidence of significant seasonal variation in EBNA IgG, EBV VCA IgG or VZV IgG levels, however antibody levels did change over the course of the year. EBNA IgG was not significantly predicted by UVR dose (OR = 0.87, $p = 0.61$) or vitamin D (OR = 0.98, $p = 0.40$). UVR dose did not significantly predict EBV VCA IgG (OR = 1.09, $p = 0.43$), nor did vitamin D (OR = 1.03, $p = 0.74$). UVR dose significantly predicted VZV IgG levels ($\beta = 31.09$, $p = 0.002$), although vitamin D did not ($\beta = 4.31$, $p = 0.08$). The positive relationship between UVR dose and immune marker concentration suggested that for every increase in UVR of one SED, immune marker levels increased by 31.09mIU/mL (95% CI 11.46 - 50.72). This association held after adjustment for age which also significantly predicted VZV IgG concentration.

Discussion

Ultraviolet radiation (UVR) and vitamin D status are recognized as modulators of immune function and are implicated in the maintenance of adequate but not overzealous immune responses and it was hypothesised that immune function would vary seasonally, as well as with variation in vitamin D status or personal UVR dose across the year. Although the immune marker levels showed variation across the year with differences between seasons (Figure 1), no significant seasonal trend was found. Despite

this, there was a significant decrease in immune marker levels between summer and autumn, and an almost significant decrease between summer and winter for VZV IgG. This pattern was consistent with seasonal patterns observed for UVR dose. Nonetheless, the decrease in antibody concentration in autumn and winter is consistent with some aspect of seasonal variation affecting T cell function. Overall, no significant relationship was found between immune marker levels and mean 25(OH)D concentration. However, all three immune markers did have a significant association with age, with EBNA IgG and EBV VCA IgG levels increasing with age, and VZV IgG levels decreasing with age.

Of the three immune markers analyzed, only VZV IgG levels were significantly associated with UVR dose. This relationship held after adjustment for age (and other potential confounders), which were also significantly associated with IgG levels of all three immune markers. This relationship suggested that with every increase in UVR dose immune marker concentration also increased, indicating that UVR may be stimulating the adaptive immune system. The incidence of Varicella Zoster infection (chickenpox) has a noted seasonal distribution (Norval 2006) which may make it a more suitable candidate for examining seasonal variation of adaptive immunity, particularly because most people encounter it before they are aged 15 years (Chant *et al.* 1998).

The results here could represent that higher UVR levels are not specifically immunosuppressive, but immunomodulatory to optimize immune responses to threats. UVR doses measured in this study were generally relatively low (Herlihy *et al.* 1994) but had a large range from 0 – 47.05 SEDS. These results may suggest that immune function has a U-shaped association with sun exposure, where very small increases in levels are immunosuppressive, but very large doses of UVR are stimulatory. It is not clear whether higher levels of Th1 function in healthy people suggests that they have a more efficient immune response, or whether it is actually causing over-response which may prove harmful.

This study was limited to data collected from October 2012 to July 2013, therefore little data for Spring were available and this may have implications for the seasonal trends observed. However, this study is supported by very accurate data on UVR provided by ARPANSA. Combined with state of the art 25(OH)D assays, the data analyzed are highly accurate. It would be of benefit to the study to reanalyze the data when collection is complete to accurately assess the pattern of immune marker variation over all seasons and co-variation with vitamin D and sun exposure.

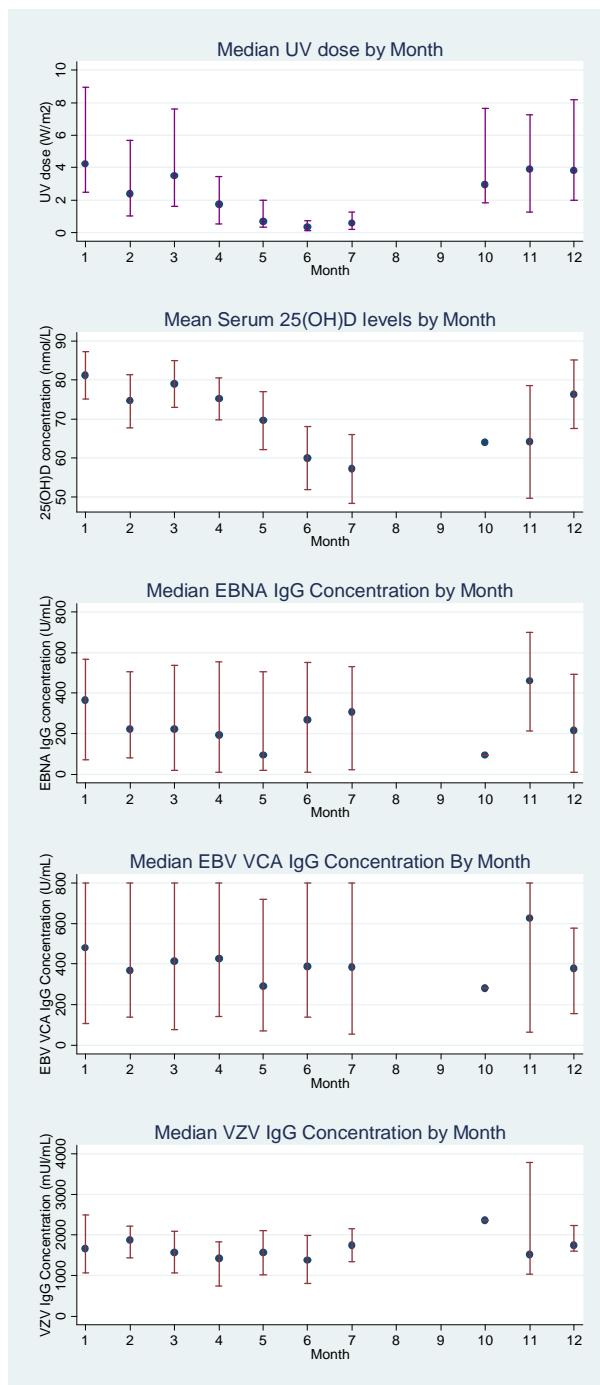


Figure 1. Mean 25(OH)D levels and median levels of UVR dose, and immune markers across one year

Conclusion

Levels of antibodies to some common infections vary across the year but not significantly. UVR dose but not 25(OH)D level had a role in modulating the adaptive immune system, consistent with other research. The positive association observed between UVR dose and VZV IgG differs from the generally accepted hypothesis that UVR is

immunosuppressive. This suggests that UVR exposure may play a modulatory role (rather than an immunosuppressive role) to protect against overzealous immune responses.

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