Elevated C-Reactive Protein: An Inflammation Indicator Due to Low-Quality Sleep

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Disclaimers: The views expressed in this article are the lead author's and not an official position of LLU, SPH. The authors have no potential conflicts of interest regarding the research, authorship, or publication of this article.

Abstract

Background: High inflammation levels and obesity are each linked to worse health outcomes. Low-quality sleep is linked to higher inflammation.

Method: This cross-sectional study investigated whether: individuals with low-quality sleep have higher inflammation; regardless of BMI; low-quality sleep interacts with BMI regarding cross-sectional prediction of inflammation; and whether sleep quality questions could identify this association. We utilized linear regression with 500 African American and Caucasian adults from an Adventist Health Study-2 subset, who completed additional biological indicator testing.

Result: Higher total sleep disturbance (TSD) was associated with increased C-reactive Protein (CRP), p = 0.008, (95% CI = 0.22 to 1.42). The interaction of TSD and BMI was significant in a curvilinear association, p = 0.018, (95% CI = -0.05 to -0.01). As TSD increased, CRP increased; however, the association existed primarily in obese individuals (BMI >30). Low-quality sleep is associated with increased CRP levels, which is a consistent inflammation indicator.

Conclusion: Obesity was not a risk factor for significantly increased CRP until sleep disturbance was indicated as "often" or "almost every day". This study supports asking sleep quality questions in primary care, for early identification of risk.

Keywords: Sleep quality, C-reactive protein, obesity, inflammation, cross-sectional, sleep disturbance, body mass index, sleep questions, primary care, United States

Introduction

Evaluating sleep health is a missing key to diagnosing, assessing, and treating chronic health problems. Low-quality sleep is associated with more chronic inflammation, while high-quality sleep helps to protect an individual from chronic health problems, even if that individual is categorized as obese (Gaines et al., 2018). However, an individual's body mass index (BMI) may not always indicate the level of inflammation inside the body or estimate the true health of that individual (Ding et al., 2016).

Obesity is a costly disease, but not all of those who are obese have chronic health problems (Ding, Chan, & Magkos, 2016; Engin, 2017; Lin, Zhang, Zheng, & Zheng, 2017; Wolfenden, Ezzati, Larijani, & Dietz, 2019). Just identifying and treating one sleep quality health problem, obstructive sleep apnea (OSA), helped Union Pacific Railroad save nearly 5 million dollars in the four years of their study (Potts et al., 2013). Jennum and Kjellberg (2011) identified that untreated OSA is present eight years prior to being treated, significantly raising medical and socioeconomic costs (Jennum & Kjellberg, 2011).

Assessing sleep quality challenges in primary care can significantly increase identification of patients with sleep problems earlier (Budhiraja, Thomas, Kim, & Redline, 2016; Guilleminault, Kirisoglu, & Ohayon, 2004; Jaiswal, Owens, & Malhotra, 2017). Identifying sleep quality problems early can also help decrease long-term health problems and the significant associated costs (Jennum & Kjellberg, 2011; Potts et al., 2013).

Inflammation and C-Reactive Protein

High levels of inflammation in the body are a common challenge for individuals with chronic health problems and low-quality sleep. C-reactive protein (CRP) is a consistent indicator of inflammation inside the body and predicts chronic disease in individuals with short and long sleep and with individuals that exhibit low-quality sleep (Grandner, Sands-Lincoln, Pak, & Garland, 2013; Huang et al., 2021). The lack of high-quality sleep is also correlated with exacerbation of chronic health problems (Walker, 2017). When an individual does not have high-quality sleep, it leads to a positive correlation to increased inflammation inside the body and higher CRP and interleukin 6 (IL-6) levels (Huang et al., 2017). The inflammation associated with low-quality sleep is also correlated with increased cortisol, monocyte count and other inflammatory indicators (Floam et al., 2015). Higher inflammation levels have been identified, regardless of what a patient's BMI or waist circumference happens to be, when the individual exhibits low quality sleep (Huang et al., 2021). Levels of cortisol are significantly increased among men with low sleep quality (Bassett et al., 2015). Additionally, low sleep quality is associated with significantly higher cortisol levels that are sustained for a significantly longer length of time regardless of age, gender or ethnicity (Castro-Diehl et al., 2015; Massar, Liu, Mohammad, & Chee, 2017).

Sleep Quality

Health care providers rarely ask quality of sleep related questions during routine healthcare visits, even though high-quality sleep is considered pivotal for good long-term health (Jaiswal et al., 2017). Comparing patients with and without sleep problems, patients who have even one sleep problem are hospitalized more, access home-health care more, and utilize more health care services (Kaufmann et al., 2013). Additionally, individuals with two or more sleep problems have increased nursing home utilization costs (Kaufmann et al., 2013). If sleep quality were assessed at each clinical visit in the same way that blood pressure is assessed as a vital sign, chronic health problems might be averted, treated earlier or at least delayed from occurring.

Research Aims and Study Design

The research aims were to determine whether: (a) individuals with low-quality sleep have higher levels of abnormal inflammatory responses; (b) individuals with low-quality sleep have higher inflammation levels regardless of BMI; (c) low-quality sleep interacts with an individual's BMI regarding the cross-sectional prediction of inflammation; and (d) whether sleep quality questions can identify the association between low-quality sleep and increased inflammation.

This study data came about due to increased interest in identifying whether there were differences in mental and physical health outcomes for those who were religious or spiritually inclined, and the recommendation that more subpopulation research in various religious groups be undertaken, as described in Lee, et. al., 2009 (Lee et al., 2009). Some of the pertinent data was already available in the larger Adventist Health Study-2 (AHS-2), but for the biological data, this required additional testing and obtaining biological specimens from a smaller subset, due to the expense. Hence the Biological Manifestations of Religion and Health Study (BioMRS) was started (Lee et al., 2009). This study was observational and used a cross-sectional design. This research was approved by the Internal Review Board (IRB) of Loma Linda University Medical Center (LLUMC), Loma Linda, California, USA.

Methodology

The parent study, the AHS-2, began in 2002 to investigate which foods might change cancer risk (Butler et al., 2008). Adventists were chosen for this National Institute of Health (NIH) research because a large portion of Adventists

typically follows a vegetarian or semi-vegetarian diet, in addition to being a mostly smoke-free and alcohol-free population (Butler et al., 2008). Additionally, there are a significant number of African Americans in the United States (US) and of African descent in Canada who are Adventist, which enabled a broader, more balanced evaluation of cancer-related diet risk in this part of North America (Butler et al., 2008). The AHS-2 sample included Adventist members who were age 30 or older, and who were proficient in English, with more than 96,000 members in the first wave of data collection (Butler et al., 2008). The participants were invited to join the research study via information given in Adventist churches in every region of the US and Canada during a 7 to 8-week promotion (Butler et al., 2008). All aspects of informed consent and ethical considerations were followed in the study, per the Loma Linda University Health requirements.

The Biopsychosocial Religion and Health Study (BRHS) began in 2006 to identify whether there were positive or negative, mental and physical health changes that occurred for those who were religiously or spiritually inclined (Lee et al., 2009). There were 20,000 AHS-2 participants older than age 35, randomly sampled and mailed a 20-page religion and health questionnaire, with more than 11,000 participants returning the questionnaire (Lee et al., 2009). Within the BRHS is the subset of the 500 BioMRS participants who gave additional time in donating biological samples and answering questions to help determine "how manifestations of religious experience relate to biologic indicators of allostatic load within the context of cumulative risk exposure" (Lee et al., 2009, p. 1471). The African American and Caucasian BioMRS participants were invited initially through a letter and then a phone call, and only a small sample size was recruited due to the high cost to complete this study (Lee et al., 2009). All aspects of informed consent, and ethical considerations were followed in the study, per the Loma Linda University Health requirements. Sleep quality was one of the items evaluated, to help determine allostatic load risk, which we utilized in this study.

Participants and Study Size

The study data was obtained from the Biological Manifestations of Religion and Health Study (BioMRS), a part of a larger National Institute on Aging-funded study—the Biopsychosocial Religion and Health Study (BRHS-1R01AG026348) (Lee et al., 2009). The first BioMRS wave occurred from 2006 to 2007 with 536 participants, while the second wave occurred between 2010 and 2011 and involved 298 participants. The BioMRS study is a subset within the Adventist Health Study 2 (AHS-2), a longitudinal, NIH-funded epidemiological study (AHS-2-R01CA094594) (Butler et al., 2008). The BioMRS study participants are all participants of the larger AHS-2 longitudinal study who lived near LLUMC and were able to drive to LLUMC, donate blood and other specimens, and answer research questions. The BRHS staff invited all previous AHS-2 participants (several years before our study) who lived close enough to the clinics, to join the BioMRS study via letter and phone call. The California clinic areas included: Loma Linda, Riverside, and Los Angeles. The BioMRS study size was determined based on the availability of AHS-2 participants within driving distance of the study clinic sites. The mean age of participants was 69.3 ± 11.6 years. The mean education level was a bachelor's degree, and the mean basic financial needs (the challenge of the ability to afford necessities in the previous year) were between "*not at all*" and "*a little*" of a problem.

Measurement, Validity, and Reliability

Inflammation. The dependent inflammatory indicators evaluated were: C - reactive protein (CRP), Interleukin 6 (IL-6), and urine cortisol. The BioMRS inflammatory variables: CRP, IL-6, and urine cortisol were measured in the LLUMC School of Medicine lab with ELISA kits from R & D Scientific. The blood work was done in the School of Medicine Lab after participants had fasted for 12 hours. The urine cortisol was a 12-hour fasting urinary cortisol to ensure compliance across all participants, similar to the work done by Dr. Blackburn, (Fair et al., 2017; Tomiyama et al., 2012).

Sleep. The three sleep quality questions and scoring were previously validated in Kaplan's 1999 Alameda County Health and Ways of Living Study (Kaplan, 2006). The Cronbach's alphas for the sleep quality questions in wave*s* 1 and 2 were .784, and .791. We evaluated participant self-reports on three sleep quality questions. The questions were asked with the leading explanation of "During the past 4 weeks, how often would you say you have had any of these problems related to your sleep": (a) "Trouble falling asleep", (b) "Waking up in the middle of the night and finding it hard to get back to sleep", and (c) "Waking up very early and can't get back to sleep".

Total sleep disturbance was calculated as the total sum of the self-reported sleep quality questions: (a) trouble falling asleep, (b) trouble staying asleep, and (c) trouble waking up early. The scores for each of the three sleep quality questions ranged from 0 to 3, with sleep problems rated 0 = *rarely or never,* 1 = *sometimes,* 2 = *often, and* 3 = *almost every day*. The total sleep disturbance score was a total of the three sleep questions, with a total score range of 0 to 9. For graphing purposes, the sleep quality scores were adjusted to be 1 to 4, for a total sleep disturbance score of 3 to 12. The test-retest reliability value for total sleep disturbance score was .640, ($p <$ .001).

Body Mass Index (BMI). Weight was determined using the scale function of the Tanita Body Fat Analyzer and height was measured using a portable stadiometer. BMI was calculated as weight (kg)/height (m^2). Participants were asked to remove their shoes, heavy outer garments such as jackets and cardigans, heavy jewelry*,* loose money*,* and keys from their pockets before their weight and height were determined. The weight values for BMI were*,* lean = below 18.4 kg/m^2; normal = 18.5 to 24.9 kg/m^2; overweight = 25.0 to 29.9 kg/m^2; and obese = over 30.0 kg/m^2 (National Heart & Institute, 1998). The control variables included: age, gender, ethnicity, and basic needs (the ability to pay for needed expenses in the one-year prior).

Statistical Analysis

A generalized linear model was used for analysis with IBM SPSS Statistics 26 (Corp., 2019). Multiple imputation, with five imputations, was used for missing data, although less than 5% of the data was missing. Each variable (age, gender, ethnicity, basic needs, total sleep disturbance, squared sleep disturbance, total sleep hours, squared sleep hours, and BMI) was put into the model with main effects. Interactions were evaluated between BMI and each of the following: total sleep disturbance, squared sleep disturbance, total sleep hours, and squared sleep hours. A robust estimator was used for parameter estimation. Exponential parameter estimates were included with model effects to test for curvilinear associations. The predicted value of the linear predictor was saved for graphing analysis. Age, gender, ethnicity, and the ability to afford basic needs were controlled in the statistical analysis, to address potential sources of bias. CRP, IL-6 and urine cortisol were log-transformed prior to statistical analysis due to their deviation from a normal distribution.

Results

There were 500 African American and Caucasian participants in this study, (some participants preferred not to have ethnicity categorized, although only African American and Caucasian participants were included in the study); participants self-reporting as "Caucasian" were 278 individuals; participants self-reporting as "African American" were 188 individuals and 34 individuals self-reported as "Other" to stay anonymous. The gender self-reports were 63% female and 37% male. See Table 1 for missing data which included: the three inflammation indicators included in this study C-reactive protein, interleukin-6 and urine cortisol; the three sleep quality questions and total sleep hours; body mass index; and participant identifiers of age, gender and ethnicity; and financial stress as shown with basic need level. See Table 2 for participant characteristics which included: the average total and squared sleep disturbance; the confounder of education that was controlled for in analysis; age and BMI are self-explanatory; C-reactive protein, which is the significant inflammation indicator; and then a breakdown of gender and ethnicity with BMI and total sleep disturbance. The majority of the participants in the parent study were either African American or Caucasian since the original AHS-2 study was funded by the National Cancer Institute to

examine health disparities, and there were insufficient funds in AHS-2 to obtain large enough sample sizes of other ethnicities to make such comparisons.

Table 1
Missing Data of Total Sample Size

Variable	Total Missing
C-reactive Protein	14
Interleukin 6	14
Urine cortisol	21
Q#1 Fall Asleep	4
Q#2 Stay Asleep	3
Q#3 Wake Early	6
Total sleep hours	13
Age & gender	2
Ethnicity	34
Body mass index	43
Ability to meet basic needs	12

Table 2
Participant Characteristics

Characteristics of the Sample (N = 500)		
	Mean	SD
Age	69.26	11.56
TSD1 Mean [a]	5.03	2.07
Squared TSD1 Mean	29.64	26.31
BMI	26.69	4.98
Education [b]	6.75	1.74
Basic Needs [c]	1.35	0.88
Log CRP in mg	2.99	0.55
	n	*Percent*
Gender		
Females	313	62.9
Caucasian	159	34.1
African American	130	27.9
Males	185	37.1
Caucasian	119	25.5
African American	58	12.4
Ethnicity		
Caucasian	278	55.6
African American	188	37.6
TSD1		
1	157	31.4
2	240	48.0
3	77	15.4
4	18	3.6
BMI totals		
Lean = < 18.4	4	0.8
Normal = 18.5—24.9	184	36.8
Overweight = 25.0—29.9	172	34.4
Obese = > 30.0	89	17.8

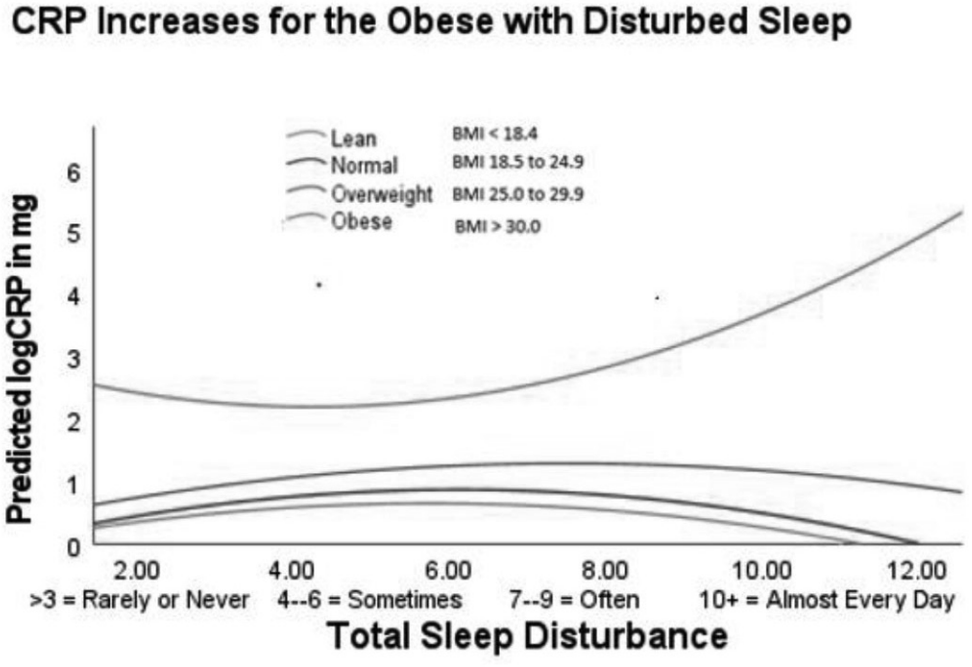
Note. [a]1 = "Rarely or Never", 2 = "Sometimes", 3 = "Often", 4 = "Almost Every Day"; the TSD1 = adding all three scores together for a total score of 3 to 12.
[b]1 = "Grade School", 2 = "Some High School", 3 = "High School Diploma", 4 = "Trade School Diploma", 5 = "Some College", 6 = "Associate Degree", 7 = "Bachelors Degree", 8 = "Master's Degree", 9 "Doctoral Degree"
[c]1 = "Not at all", 2 = "A little", 3 = "Somewhat", 4 = "Fairly" (often), 5 = "Very"

Most participants did not smoke or drink alcohol or caffeinated beverages, which helped decrease potential confounders for sleep quality. Eighty percent of the participants reported that they had never drunk alcohol. Only four had drank any alcohol in the previous twelve months, and the frequency was less than 1 drink per month for the majority. No one reported currently smoking, only 1 individual had smoked in the previous twelve months, and only 4 individuals reported ever smoking. Regarding caffeine, 62% self-reported never or rarely (less than once per month) drinking any caffeinated beverage, 10% drank one caffeinated beverage daily, and only 6 percent drank more than one caffeinated drink per day.

Research Aims 1 and 2

Figure 1 shows that when obese individuals have low-quality sleep occurring "often" or "almost every day", their CRP inflammation levels are higher. Whereas, when an obese individual has high-quality sleep, the CRP inflammation levels are closer to those in normal and overweight individuals. Low-quality sleep in the normal-weight, under-weight and over-weight categories did not show increased CRP levels with low-quality sleep.

Figure 1
The Association of Total Sleep Disturbance with CRP for Different BMI Groups



Research Aim 3

Table 3 shows that low-quality sleep interacts with an individual's BMI and inflammation risk with CRP inflammation level. A higher total sleep disturbance was associated with increased CRP, p = .008, (95% CI = 0.22 to 1.42). The interaction of total sleep disturbance and BMI was significant, p = .018, (95% CI = -0.05 to -0.01). Males had a lower CRP level, $p < .001$, (95% CI = -0.30 to -0.12), as compared to females, but ethnicity was not significant, p = .465, (95% CI = -0.07 to 0.14). The interaction between BMI and squared sleep disturbance was significant, p = .005, (95% CI = 0.00 to 0.00).

The interaction between BMI and squared sleep disturbance in predicting CRP is also shown in figure 1. For most participants, total sleep disturbance did not show a relationship between sleep

quality and CRP. However, for those individuals who were obese, total sleep disturbance had a curvilinear relationship with CRP. Starting with the sleep disturbance of about seven (sleep disturbance occurring "often"), there was a gradually increasing relationship between sleep disturbance and CRP. The CRP level was highest for obese individuals when total sleep disturbance was above 7 on a scale of 3 to 12, $p = .008$, (95% CI = 0.22 to 1.42). The category of obese was classified as a BMI over 30 kg/m^2 per the National Heart, Lung and Blood guidelines (National Heart & Institute, 1998). The low BMI, normal BMI and overweight BMI ranges did not show a tipping point increase for total sleep disturbance with CRP.

Table 3
Regression of Log CRP on Sleep Disturbance, BMI, and Controls.

"Regression of log CRP on Sleep disturbance, BMI, and Controls"

Parameter	B	95% Wald Confidence Interval		*p*
		Lower	Upper	
(Intercept)	-0.61	-7.70	6.48	.863
Age	0.00	0.00	0.01	**.050**
Male	-0.21	-0.30	-0.12	**.000**
African American	0.04	-0.07	0.14	.465
Difficulty Meeting Expenses	0.00	-0.05	0.06	.901
Sleep Hours (S)	0.09	-1.96	2.13	.935
Sleep Hours Squared (S^2)	0.00	-0.16	0.15	.965
Total Sleep Disturbance (TSD)	0.82	0.22	1.42	**.008**
Total Sleep Disturbance Squared (TSD^2)	-0.07	-0.12	-0.03	**.002**
BMI (B)	0.14	-0.10	0.37	.249
S × B	-0.01	-0.08	0.06	.799
S^2 × B	0.00	0.00	0.01	.820
TSD × B	-0.03	-0.05	-0.01	**.018**
TSD^2 × B	0.00	0.00	0.00	**.005**

S = Sleep Hours S^2 = Sleep Hours Squared TSD = Total Sleep Disturbance

TSD^2 = Total Sleep Disturbance Squared B = Body Mass Index

Research Aim 4

Sleep quality questions were able to identify the association between low-quality sleep and increased inflammation risk for those individuals who were obese. Sleep quality questions could be useful in primary care to help identify obese individuals with low-quality sleep.

Additional findings of this study

Males exhibited lower CRP levels compared to females. This finding is similar to what other researchers have identified, with females exhibiting and/or self-reporting worse sleep quality over their lifetime (Nowakowski et al., 2018). Two other inflammatory variables were evaluated: Interleukin 6 (IL-6) and urine cortisol with both only significant for the control variables, ethnicity, and age. A higher IL-6 was associated with older age and among African American participants, $p = .024$. A higher urine cortisol level was associated with being older and among Caucasian participants, $p = .049$. An interesting finding of this study was that there were no significant sleep quality differences between ethnicities. The African American and Caucasian BioMRS participants appear to have similar sleep quality.

Discussion

Obese individuals with higher total sleep disturbance also had a higher CRP inflammation level. Obesity was not a risk factor for significantly increased CRP until total sleep disturbance problems were "*often*" or "*almost every day*". Males had a lower CRP level than females, but ethnicity was not significant. Sleep quality questions were able to identify the risk for increased CRP levels for obese individuals, discussed in detail below.

C - reactive protein

Study results showed that less total sleep disturbance, even among individuals with a high BMI, was associated with a lower CRP level. Even though an individual was categorized in the obese category, if that individual had high-quality sleep (as shown by a low total sleep disturbance score), their CRP inflammation levels remained closer to the range of individuals who were considered to have normal, underweight or over-weight BMI's. Higher sleep quality/lower sleep disturbance was associated with less inflammation and lower CRP levels. The study findings were similar to the 2005 to 2008 National Health and Nutrition Examination Survey (NHANES) which found elevated CRP levels in participants that exhibited low-quality sleep, however, NHANES only found elevated CRP levels in female participants (Liu et al., 2014). The NHANES study included eight sleep questions while our study included the three standard sleep questions most associated with sleep quality (trouble: falling asleep, staying asleep, and/or waking too early), to evaluate the usefulness of short quantitative sleep-quality vitals.

Chattu, et al. (2018) and Walker (2017) have summarized the literature on the association of high-quality sleep being associated with decreased inflammation and problems associated with chronic diseases like diabetes, Alzheimer's, heart disease, chronic depression and other mental health challenges (Chattu et al., 2018; Walker, 2017). Elevated CRP levels have previously been correlated with cardiovascular mortality (Singh-Manoux et al., 2017).

In this study the significant increase for low-quality sleep was a self-reported total sleep disturbance score above seven on a scale of three to twelve, as shown in Figure 1. Obese individuals only had significantly increased CRP levels when their sleep quality was low. This example of low-quality sleep shows when an obese individual would be at higher risk for chronic health problems, but if that same individual were able to obtain high-quality sleep, that could decrease inflammation inside the body and the associated risk for chronic diseases, even though the individual is categorized as obese. An aspect of the obesity paradox is when an individual is overweight/obese but does not have chronic health problems. This condition is identified in the literature as Metabolically Healthy Obese (MHO); contrasted with the individual that has normal weight but does have chronic health problems, identified in the literature as Metabolically Obese, Normal-Weight (MONW),(Lin et al., 2017). High-quality sleep leads to less inflammation in the body and lower CRP levels (Huang et al., 2017). In figure 1, the interaction of squared total sleep disturbance and BMI shows the tipping point where low-quality sleep raises the inflammation level in the body, as shown with CRP in this study. The self-reported sleep quality scores showed that when an obese individual experiences sleep problems "*often*" or "*almost every day*" they will have higher CRP levels. But when an obese individual has high-quality sleep, as shown with self-reports of sleep problems being "*rarely or never*" or "*sometimes",* then the CRP levels are lower. High-quality sleep seems to be foundational for keeping inflammation at its lowest level and is an indicator of overall health, regardless of what a person's BMI level is.

Our significant sleep disturbance findings on IL-6 and urine cortisol were just for the control variables of age and ethnicity, as described above, although Huang and colleagues showed that IL-6 is elevated when an individual has low quality sleep (Huang et al., 2017). Floam and colleagues identified that low sleep quality is significantly associated with increased cortisol levels and significantly higher inflammation in the body (Floam et al., 2015).

Sleep Quality

This study shows that sleep quality is an important indicator of health. Sleep quality is typically measured by sleep efficiency, which is defined as a percent of total sleep hours divided by the total hours in bed (Kushida et al., 2001). Kushida and colleagues (2001) identified that the presence of a low sleep efficiency can be determined by a patient's sleep quality answers on a sleep questionnaire (Kushida et al., 2001). Additionally, Akerstedt and colleagues (2016), as well as Cole and colleagues (2006) found that actigraphy and polysomnography results were equal to subjective sleep quality questionnaire results (Akerstedt et al., 2016; Cole et al., 2006). An individual will exhibit high-quality sleep when they can naturally fall asleep within 20-30 minutes, be able to go back to sleep within 20-30 minutes (if they awake in the middle of the night), and wake up feeling rested; plus they can sleep at least 5 ½ and up to 8 ½ hours each night (Akerstedt et al., 2016; Cole et al., 2006; Kushida et al., 2001). The three sleep quality questions in our study identify an individual's sleep efficiency level in an economic and significant way for identifying increased CRP levels. This is significant because high CRP levels are linked to increased risk for sleep-disordered breathing, heart disease and other chronic inflammatory health problems (Punjabi & Beamer, 2007; Singh-Manoux et al., 2017). Sleep quality is one of the most important healthy-sleep indicators of all the sleep parameters and can be accurately assessed with sleep quality questions.

Future intervention trials with sleep-health education may be able to reduce sleep quality problems and CRP inflammation levels. Additional future research interventions that evaluate asking sleep quality questions in primary care, may be able to identify low-quality sleep problems early, similar to the workplace interventions that identified just one low-quality sleep problem early, saving nearly 5 million dollars in four years (Potts et al., 2013). Asking sleep quality questions in primary and specialty care may save significant healthcare dollars by identifying sleep health problems earlier, and also identifying the obese patients that fit into and help explain the obesity paradox.

Limitations

The cross-sectional design of this study did not allow for determining causal predictive effects for low sleep quality and risk for higher inflammation. The study participants are homogenous in several ways: they are more likely to practice healthy behaviors, have a common Adventist faith, and are North American adults which might decrease generalizability for individuals outside of North America. There could also be a selection bias of active church members, as participants were initially notified of the parent study in a church setting.

Strengths

This study has high generalizability for various age groups, ethnicities, and sexes residing in North America. The BioMRS participants were African American and Caucasian adults aged 37 to 103 years old. The study participants also exhibited significantly less confounders that needed to be controlled for when evaluating sleep quality, as the participants in this study typically follow a healthy overall lifestyle that does not include drinking alcohol, smoking, or ingesting large amounts of caffeine (Butler et al., 2008).

Conclusion

This study showed that self-reported, low-quality sleep is associated with increased CRP levels in the obese. CRP is a consistent indicator of inflammation in the body regardless of ethnicity. Higher CRP levels were more of a problem for the obese when total sleep disturbance was reported as "*often*" or "*almost every day.*" This study supports utilizing sleep quality questions in primary care to help identify when an obese individual might be at increased risk for more chronic health problems and when the cost of caring for an obese individual could also increase.

Authorship

Study concept and design: All authors. Data acquisition: J.W.L. Data analysis: K.V.W., A.N., J.W.L. Interpretation: K.V.W., A.N., J.W.L. Analyses support. K.V.W., A.N., J.W.L. Manuscript draft: All authors. Revised manuscript: all authors.

Acknowledgements

The data for this study was supported by grants from the National Institute on Aging (Biopsychosocial Religion and Health Study, 1R01AG026348) and the National Cancer Institute for the parent study (Adventist Health Study 2, 5R01 CA094594).

Sources of Support

The original supporting research was funded by the National Institutes of Health and the National Cancer Institute.

Funding

The authors received no financial support for this research, authorship or publication of this article. The previous AHS-2 and BRHS research was funded by the National Institutes of Health.

Declaration of Interest

The authors have no potential conflicts of interest regarding the research, authorship or publication of this article.

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