



Religion, Spirituality and Risk of Coronary Heart Disease: A Matched Case–Control Study and Meta-Analysis

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Abstract

Although the association between religion/spirituality (R/S) and psychological outcomes is well established, current understanding of the association with cardiovascular disease remains limited. We sought to investigate the association between Islamic R/S and coronary heart disease (CHD), and place these findings in light of a meta-analysis. In this case–control study, 190 cases with non-fatal CHD were identified and individually matched with 383 hospital-based controls. R/S was measured by self-administered 102 items questionnaire. A tabular meta-analysis was performed of observational studies on R/S (high level versus low level) and CHD. In addition, a dose–response meta-analysis was conducted using generalized least-squares regression. Participants in the top quartile had decreased odds of CHD comparing to participants in the lowest quartile of religious belief (OR 0.20, 95% confidence interval (CI) 0.06–0.59), religious commitment (OR 0.36, CI 95% 0.13–0.99), religious emotions (OR 0.39, CI 95% 0.18–0.87), and total R/S score (OR 0.30, CI 95% 0.13–0.67). The meta-analysis study showed a significant relative risk of 0.88 (CI 95% 0.77–1.00) comparing individuals in high level versus low level of R/S. In dose–response meta-analysis, comparing people with no religious services attendance, the relative risks of CHD were 0.77 (CI 95% 0.65–0.91) for one times attendance and 0.27 (CI 95% 0.11–0.65) for five times attendance per month. R/S was associated with a significantly decreased risk of CHD. The possible causal nature of the observed associations warrants randomized clinical trial with large sample size.

Keywords Religion · Spirituality · Coronary artery disease · Systematic review · Meta-analysis

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Introduction

Cardiovascular disease (CVD) is the most important cause of death in both developed and developing countries (Go et al. 2014; Nabel and Braunwald 2012) with coronary heart disease (CHD) being the most prevalent type of CVD (Ross 1999). Despite substantial research on this topic, the disease incidence remains high, prompting continued efforts to identify psychological and social-related factors (Ladwig et al. 2014). In recent years, an increasing number of studies have examined the association between religious involvement and health outcomes (Das and Nairn 2016; Nazarzadeh et al. 2015). Although the association between religious involvement and health outcomes are well established (Koenig 2012), but current understanding of the association with major outcome such as cardiovascular disease is limited.

Several clinical trials (Ikedo et al. 2007) and observational studies (Feinstein et al. 2010; King et al. 2002) have investigated associations between religion/spirituality (R/S) and risk of CVD. Also, the previous research showed that R/S affiliation may be in association with CVD biomarkers such as C-reactive protein (King et al. 2002). Nevertheless, research on R/S and CHD is still in its infancy and the relationship remains controversial, since some studies report no significant relationship (Feinstein et al. 2010; Salmoirago-Blotcher et al. 2013) and others reported positive or negative relationships (Lucchese and Koenig 2013; Salmoirago-Blotcher et al. 2013).

To our knowledge, no research has yet examined associations between R/S and CHD in the Middle East region. Therefore, whether or not R/S is an associated factor for CHD risk remains unknown. The present case–control study was conducted to examine the association between R/S and CHD among Muslims in Ilam city (located in west of Iran). We hypothesize that Muslim adults with higher R/S will experience lower risk of CHD, after adjustment and matching for well-known confounders. Secondary aims of this study were to conduct a systematic review and meta-analysis of observational studies to place our findings in the context of other research.

Materials and Methods

Study Design and Population

In this hospital-based case–control study, 573 participants including 324 men and 249 women aged 18 year or over were recruited during a 2-year period from October 2013 to May 2015. Study participants were recruited from two referral hospitals located in Ilam city (west of Iran). First, 190 incidence cases of non-fatal CHD were identified from the Mostafa Khomeini hospital (the central hospital for admission of the CVD patients) and then matched to 383 controls from Emam Khomeini hospital (the only general hospital in the city). Controls were selected from patients admitted for trauma and general surgery (not related to CVD) with a case-to-control ratio of 1:2.

Case and Control Definitions

Cases were adults with non-fatal CHD referred to the above hospital. Non-fatal CHD was considered as acute coronary syndrome (ACS) or coronary arteries disease (CAD). ACS included patients with ST elevation ACS (STE-ACS) (cases with chest pain symptoms and persistent ST-segment elevation of greater than 20-min duration), non-ST elevation ACS

(NSTE-ACS) (cases with acute chest pain symptoms but without persistent ST-segment elevation), unstable angina (UA) (NSTE-ACS + normal troponin levels), and non-ST-elevation MI (NSTEMI) (NSTE-ACS + increased troponin levels). CAD was defined as 50% or greater coronary lumen stenosis of any coronary vessel. Two matched controls (with no history of CVD) were sought for each case. Matching was by age (± 2.5 year interval) and gender.

Inclusion and Exclusion Criteria

Inclusion criteria were all CHD cases residing in Ilam city (and cities within less than 100 km from Ilam city) who referred to Mostafa Khomeini hospital during the study period. CHD patients were diagnosed by an expert cardiologist based on the above definitions. Control group were selected from patients who admitted to the above-mentioned general hospitals. Exclusion criteria were: (1) history of underlying disease (diabetes, hypertension, prior CHD, and stroke), (2) the presence of self-report psychological disorders (depression, obsessive compulsive disorder, anxiety), and (3) non-Muslims. Participants signed their written informed consent form to participate in this study. The signed forms were archived in a confidential place in the department. The methodology and questionnaire of the present study was approved by central ethic committee of the Ilam University of Medical Sciences.

Variables and Measurements

A single trained nurse in each hospital interviewed the participants. The main exposure variable was Islamic religion/spirituality (R/S) which was measured as the following. Total R/S and three of its dimensions were measured by the “Persian religiosity scale questionnaire” (RSQ), developed to measure Iranian Muslims R/S. The psychometric characteristics of the scale have been described elsewhere (Khodayarifard and Rahiminejad 2009). Briefly, this questionnaire consists of 97 questions measuring three dimensions of R/S in Islam including religious belief, religious commitment, and religious emotions. The RSQ also includes five questions to identify individuals who are presenting themselves as more religious than they really are (i.e., providing socially desirable responses). Scoring of the RSQ items was based on Likert’s scale with six options that range from “highly disagree” to “highly agree.” The religious belief dimension consists of 48 questions measuring belief and knowledge about God, Prophets, Islamic Imams, resurrection, religious observance, and the Quran. The religious commitment dimension was assessed by 26 questions about frequency of private worship, social worships, individual ethics, social ethics, and interactions with nature. The religious emotion dimension was measured with 23 questions that assess emotions toward God, emotions toward the Prophets and Islamic Imams, kindness to family and people, moral virtues, dislike of immoral behavior, and dislike of enemies of God. A total R/S score is obtained by summing the three dimensions.

Bias and Confounding

Controls were selected in a way that would balance probable recall bias between case and control in the measurement of R/S (Yates et al. 2005). Recall bias in the present study means false increase in R/S scores after severe disease and hospitalization. In an effort to balance this bias between the cases and controls, we recruited controls through hospitalized

patients with similar disease severity but without CVD history. In addition, cases and controls were matched individually based on age and sex as well-known confounders (Powell et al. 2003).

Statistical Methods

Odds ratios (OR) were estimated using conditional logistic regression to assess the association between R/S and CHD. Confounder variables were selected based on whether they were associated with R/S, CHD, or both. For each R/S dimension (religious belief, religious commitment, religious emotions, and total R/S score), three models were fitted. First, R/S dimensions were considered as continuous variable and then they were categorized based on quartiles ($< Q1$, $Q1-Q2$, $Q2-Q3$, and $> Q3$) for assessing any deviation from linearity. Model 1 was adjusted for family history of CVD, smoking, and passive exposure to smoking; Model 2 adjusted for model 1 plus birth place, marital status, educational level, job category, and past medical history; and Model 3 adjusted for model 2 plus fasting blood sugar (FBS), high-density lipoprotein (HDL), triglyceride (TG), total cholesterol (TC), low-density lipoprotein (LDL), systolic blood pressure (SBP), and diastolic blood pressure (DBP). Potential multicollinearity was assessed using a tolerance of 0.1 or less (or variance inflation factor of 10 or greater). A dose–response relationship was assessed using a restricted cubic spline model (Orsini and Greenland 2011) with three knots at the 25th, 50th, and 75th percentiles of R/S scores after adjustment for all confounders. The reference category was the lowest scoring quartile of R/S dimensions. Wald test for nonlinearity calculated by testing the regression coefficient of the second spline equal to zero. All the statistical analyses were performed using Stata/MP 14.1 for windows.

Systematic Review, Tabular Meta-Analysis and Dose–Response Meta-Analysis

In order to place the results of this study in the context of other observational research, we conducted a systematic review to identify all the observational studies that assessed the association between R/S and CVD. We searched three electronic databases including PubMed, PubMed Central, and Psych Info (without language or time limitations) up to April 2016. The search strategy consisted of keywords related to R/S combined with specific terms for CHD. All published papers from observational studies that reported adjusted measures of association (odds ratio, rate ratio, risk ratio) between R/S and CHD were eligible. All interventional studies, review articles, studies without a control group, and papers that considered other cardiovascular disease as outcomes were excluded from the review. The following information was extracted from the eligible studies: author name, year of publication, age, sex, study design, sample size, CHD case number, questionnaire type and internal consistency, total participants, R/S definition, outcome definition, and measure of association. With considering the rare disease assumption ($< 5\%$) (Vandenbroucke and Pearce 2012), adjusted OR and RR were combined in the meta-analysis using a random and fixed effect model. Random-effect multivariate meta-regression model was used to evaluate the effect of mean age, year of publication, type of studies (case–control and cohort), and level of adjustment on heterogeneity. We employed a permutation-based method suggested by Higgins and Thompson (Harbord and Higgins 2008; Higgins and Thompson 2004) in calculating p values. This method was recommended in two important conditions: (1) small number of studies included in the meta-regression model and (2) for controlling type I error when more than one covariate was

present in a meta-regression model (Harbord and Higgins 2008). In addition, the Cochran's Q test, I^2 , and τ^2 statistics were conducted to determine the presence of heterogeneity among studies. The Egger's tests were used for assessing the publication bias.

In dose–response meta-analysis, summary information of the cases number, total sample size or total person-time within each category of exposure is needed. Dose–response meta-analysis method of Greenland and Longnecker was used to estimate the log RR per each time increase in religious services attendance in a month (Greenland and Longnecker 1992). The restricted cubic spline model with three knots at the 25th, 50th, and 75th percentiles of frequency of attendance at religious services was used to assess the potential nonlinear relationship in meta-analysis (Orsini et al. 2006).

Results

Case–control study

The R/S data were obtained from 190 of the 200 enrolled cases (10 cases were excluded because of missing data) and for 383 matched controls. The mean age of cases and controls was 55.5 ± 14.7 years, and gender was 56.3% men and 43.7% women. Categorical and continuous characteristics are presented in Tables 1 and 2.

Table S1 in supplementary materials presents the distribution of CHD across increasing categories (quartile 1–4) of R/S. In these unadjusted models, a significant association between all four R/S variables and CHD odds was observed with decreasing odds associated with increasing R/S. Table 3 presents multivariable adjusted logistic models adjusted for well-known CHD risk factors. Comparing measure of association across dimensions of R/S between the top quartile and the bottom quartile, the OR for CHD was 0.20 (95% CI 0.06–0.59) for those with high religious beliefs, 0.36 (95% CI 0.13–0.99) for those with high religious commitment, 0.39 (95% CI 0.18–0.87) for those with high religious emotions, and 0.30 (95% CI 0.13–0.67) for those with high total R/S score. For all dimensions of R/S, findings remained significant except in quartile 2 for religious commitment (OR 0.62; 95% CI 0.28–1.38) and for religious emotions (OR 0.52; 0.23–1.15). Restricted cubic splines regression demonstrated a nonlinear dose–response relationship between religious belief (p for nonlinearity < 0.001), total R/S score (p for nonlinearity < 0.001) and religious commitment (p for nonlinearity 0.01) with the odds of CHD. But, the small p value (0.16) indicates no departure from linearity for religious emotion (Fig. 1).

Meta-Analysis

A total of 3267 citations were retrieved of which nine studies (Banerjee et al. 2014; Burazeri et al. 2008; Feinstein et al. 2010; Friedlander et al. 1986; Li et al. 2016; Obisesan et al. 2006; Salmoirago-Blotcher et al. 2013; Schnell et al. 2010) (including the present case–control study) totaling 238,100 participants (9709 CHD cases) met the inclusion criteria and were included in the pooled analysis (Figure S1 Supplementary). Characteristics of included studies are presented in Table S2 Supplementary. Of the nine studies, two were population-based case–control studies, one was a hospital-based case–control study, two were national cross-sectional survey, and the four others were prospective cohort studies. In this meta-analysis, the pooled RR for CHD was 0.88 (95% CI 0.77–1.00) with substantial heterogeneity among studies ($I^2 = 83.8\%$, $p < 0.001$) comparing individuals in

Table 1 Demographic characteristic of participants in case–control study

Characteristics	Cases (n = 190)		Controls (n = 383)		Total (n = 573)		Crude OR	95% CI	P ^a
	No.	%	No.	%	No.	%			
Gender									
Female	83	43.68	166	43.34	249	43.46	–	–	
Male	107	56.32	217	56.66	324	56.54	–	–	
Birth place									
Rural	49	26.49	117	31.88	166	30.07	Ref	Ref	
Urban	136	73.51	250	68.12	386	69.93	1.33	0.89–2.00	0.15
Marital status									
Single	10	5.35	43	11.29	53	9.33	Ref	Ref	
Married	155	82.89	295	77.43	450	79.23	2.95	1.28–6.78	0.01
Widow or divorced	22	11.76	43	11.29	65	11.44	2.90	1.06–7.90	0.03
Family history of heart disease									
No	131	68.95	379	98.96	510	89.01	Ref	Ref	
Yes	59	31.05	4	1.04	63	10.99	58.00	14.11–238.36	< 0.001
Educational level									
> High school	61	32.97	104	27.15	165	29.05	Ref	Ref	
< High school	124	67.03	279	72.85	403	70.95	0.73	0.47–1.13	0.16
Job categories									
Semi- and unskilled manual workers	24	12.77	108	28.20	132	23.12	Ref	Ref	
Supervisory or clerical and junior manager	43	22.87	38	9.92	81	14.19	6.88	3.20–14.80	< 0.001
Housewife	76	40.43	142	37.08	218	38.18	4.91	2.13–11.31	< 0.001
Unemployed	22	11.70	54	14.10	76	13.31	1.71	0.84–3.45	0.13
Other	23	12.23	41	10.70	64	11.21	2.99	1.48–6.03	0.002
Past medical history									
Healthy	79	41.58	233	60.84	312	54.45	Ref	Ref	
Known diabetes	17	8.95	26	6.79	43	7.50	2.10	0.97–4.57	0.05
Known blood pressure	54	28.42	58	15.14	112	19.55	3.08	1.81–5.26	< 0.001
Known diabetes and known blood pressure	38	20.00	14	3.66	52	9.08	9.71	4.47–21.06	< 0.001
Other disease	2	1.05	52	13.58	54	9.42	–	–	–
Passive smoker									
No	140	73.68	327	85.38	467	81.50	Ref	Ref	
Yes	50	26.32	56	14.62	106	18.50	2.03	1.30–3.18	0.02
Smoking									
None smoker	129	67.89	320	83.55	449	78.36	Ref	Ref	
Ever smoker	61	32.11	63	16.45	124	21.64	2.47	1.59–3.82	< 0.001

OR odds ratio, CI 95% confidence interval, P p value, Ref references category

^aThe results were calculated using univariate conditional logistic regression

Table 2 Univariate analysis comparing dimensions of religiosity/spirituality (R/S) as well as confounder variables between coronary heart disease cases and matched controls

Characteristics	Cases		Controls		Total		OR	95% CI	P value ^c
	Mean	SD	Mean	SD	Mean	SD			
Religious belief	240.87	1.39	261.67	0.42	254.40	0.84	0.37	0.23–0.58	< 0.001
Religious commitment	116.42	0.88	128.82	0.81	124.76	0.90	0.53	0.40–0.69	< 0.001
Religious emotions	111.72	0.42	119.24	0.31	116.85	0.37	0.38	0.26–0.56	< 0.001
Socially desirable responses ^a	22.37	0.13	24.90	0.11	24.01	0.13	0.13	0.07–0.26	< 0.001
Total R/S score	469.58	2.01	510.30	1.02	496.84	1.53	0.52	0.41–0.66	< 0.001
Age	55.52	14.75	55.38	14.67	55.43	14.68	–	–	
Systolic blood pressure ^b	121.51	1.20	120.30	1.12	120.30	1.16	1.72	0.42–7.05	0.45
Diastolic blood pressure ^b	74.44	1.24	74.44	1.13	74.44	1.18	0.96	0.29–3.16	0.94
Triglyceride ^b	130.32	1.63	127.74	1.40	127.74	1.49	1.12	0.67–1.86	0.65
Low-density lipoprotein ^b	95.58	1.40	84.77	1.41	89.12	1.40	3.00	1.70–5.30	< 0.001
Total cholesterol ^b	144.02	1.43	146.93	1.34	145.47	1.37	0.86	0.47–1.57	0.63
Fasting blood sugar ^b	114.43	1.41	90.01	1.27	96.54	1.33	19.74	8.49–45.86	< 0.001
High-density lipoprotein ^b	60.34	1.40	57.39	1.39	58.55	1.39	1.62	0.96–2.72	0.06

OR odds ratio, CI 95% confidence interval, P p value

^aPretending to be religious

^bLog transformation was employed and then back transformation (exponential) reported in this table

^cThe results were calculated using univariate conditional logistic regression

high level versus low level of R/S (Figure S1). Subgroup analyses based on study design showed controversial results. In case–control studies, higher R/S was associated with lower risk of CHD disease (OR = 0.69 [95% CI 0.54–0.88]; $I^2 = 60.1\%$, $P_h = 0.02$); in contrast, prospective cohort studies showed that higher R/S is in association with higher risk of CHD (RR = 1.06 [95% CI 1.00–1.11]; $I^2 = 22.6\%$, $P_h = 0.27$). The Egger's regression showed that there is no significant publication bias ($b = 0.16$, $P = 0.45$).

In the multivariable meta-regression model, I^2 was reduced by 49.89% when we included study design, mean age, year of publication, and adjustment levels in the model. After adjusting for multiple testing, there remains weak statistical evidence that the results of case–control studies differ on average from results of cohort studies ($p = 0.13$). On the other hand, meta-regression analysis of effects of mean age on the association between R/S and CHD showed that age can be an effect modifier for this association (regression coefficient = 0.026, $p = 0.02$) and the increased level of R/S is in association with decreased effect size in the age between 45 and 55 (Figure S2 Supplementary).

A total number of three studies (Burazeri et al. 2008; Feinstein et al. 2010; Salmoirago-Blotcher et al. 2013), yielding four RRs, were included in the dose–response analysis. Compared with people with no religious services attendance, the RR of CHD was 0.77 (CI 95% 0.65, 0.91) for one time, 0.59 (95% CI 0.42–0.84) for two times, 0.46 (CI 95%

Table 3 Adjusted models for relationship between religiosity/spirituality and coronary heart disease using conditional logistic regression model

Religiosity/spirituality	Model 1		Model 2		Model 3		Model 4	
	OR (CI)	P						
Religious belief								
< Q1	–	–	–	–	–	–	–	–
Q1–Q2	0.14 (0.07–0.28)	< 0.001	0.13 (0.05–0.33)	< 0.001	0.13 (0.05–0.34)	< 0.001	0.10 (0.03–0.30)	< 0.001
Q2–Q3	0.10 (0.04–0.24)	< 0.001	0.08 (0.02–0.25)	< 0.001	0.14 (0.05–0.34)	< 0.001	0.14 (0.05–0.40)	< 0.001
Q3–Q4	0.11 (0.04–0.24)	< 0.001	0.07 (0.02–0.20)	< 0.001	0.16 (0.06–0.41)	< 0.001	0.20 (0.06–0.59)	< 0.001
Religious commitment								
< Q1	–	–	–	–	–	–	–	–
Q1–Q2	0.46 (0.25–0.82)	0.01	0.49 (0.22–1.06)	0.07	0.56 (0.26–1.18)	0.13	0.62 (0.28–1.38)	0.24
Q2–Q3	0.23 (0.12–0.45)	< 0.001	0.16 (0.06–0.40)	< 0.001	0.22 (0.09–0.52)	< 0.001	0.30 (0.12–0.76)	0.01
Q3–Q4	0.14 (0.06–0.30)	< 0.001	0.12 (0.04–0.33)	< 0.001	0.27 (0.10–0.66)	< 0.001	0.36 (0.13–0.99)	0.04
Religious emotions								
< Q1	–	–	–	–	–	–	–	–
Q1–Q2	0.31 (0.16–0.60)	< 0.001	0.37 (0.15–0.88)	0.02	0.52 (0.24–1.14)	0.10	0.52 (0.23–1.15)	0.11
Q2–Q3	0.21 (0.10–0.43)	< 0.001	0.12 (0.04–0.35)	< 0.001	0.41 (0.17–0.96)	0.04	0.43 (0.18–1.00)	0.05
Q3–Q4	0.20 (0.10–0.39)	< 0.001	0.13 (0.05–0.33)	< 0.001	0.36 (0.16–0.79)	0.01	0.39 (0.18–0.87)	0.02
Spirituality total score								
< Q1	–	–	–	–	–	–	–	–
Q1–Q2	0.52 (0.28–0.94)	0.03	0.48 (0.22–1.04)	0.06	0.43 (0.20–0.93)	0.03	0.45 (0.21–0.95)	0.03
Q2–Q3	0.14 (0.07–0.30)	< 0.001	0.08 (0.02–0.24)	< 0.001	0.22 (0.09–0.53)	< 0.001	0.26 (0.11–0.61)	< 0.001
Q3–Q4	0.18 (0.09–0.36)	< 0.001	0.11 (0.04–0.29)	< 0.001	0.28 (0.12–0.65)	< 0.001	0.30 (0.13–0.67)	< 0.001

OR odds ratio, CI 95% confidence interval, P p value

Model 1: adjusted for family history of heart disease, smoking, passive smoker; model 2: adjusted for model 1 plus birth place, marital status, educational level, job categories, past medical history; model 3: adjusted for only metabolic risk factors (fasting blood sugar, high-density lipoprotein, triglyceride, total cholesterol, low-density lipoprotein, systolic blood pressure, diastolic blood pressure); model 4: adjusted for model 2 and model 3

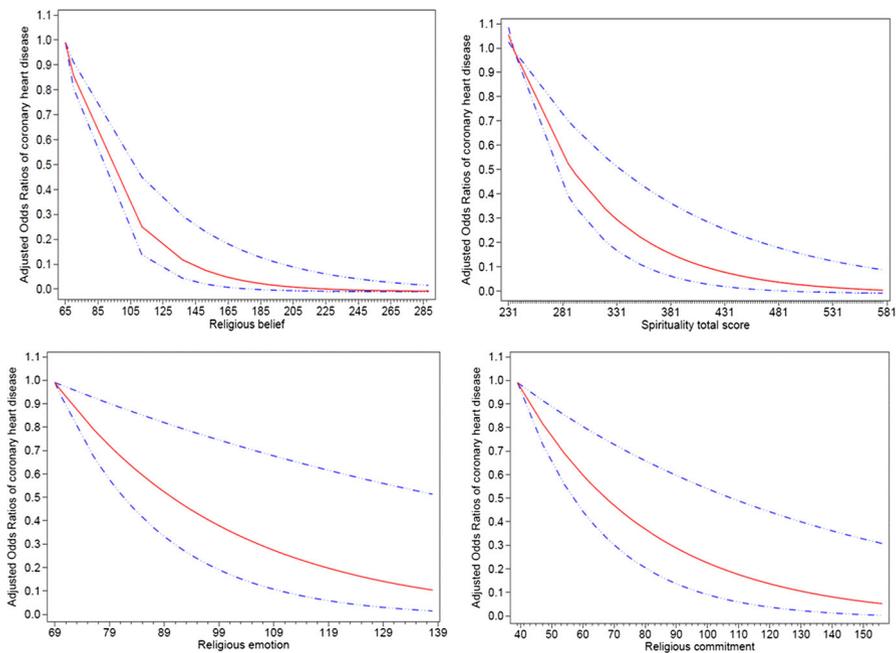


Fig. 1 Adjusted restricted cubic splines regression showing dose–response relationship between religious/spiritual dimensions and odds of coronary heart disease. Solid line represents point estimate, dotted lines are 95% confidence intervals. (p value of nonlinearity were < 0.001 for religious belief, < 0.001 for spirituality total score, 0.16 for religious emotion, 0.01 for religious commitment)

0.27–0.77) for three times, 0.35 (CI 95% 0.18–0.71) for four times, and 0.27 (CI 95% 0.11, 0.65) for five times attendance per month. The results obtained through using a restricted cubic splines model revealed a nonlinear association for religious services attendance (p values of nonlinearity < 0.001) (Fig. 2).

Discussion

This case–control study found a strong inverse dose–response relationship between increasing R/S total scores and decreasing likelihood of CHD, and a similar relationship was found for each dimension of R/S (religious belief, commitment, and emotions). Therefore, Muslims in Iran with lower R/S scores appear to be at higher odds of non-fatal CHD disease. These findings suggest that religious involvement may help to maintain cardiovascular health. In addition, our meta-analysis involving 9709 CHD cases provided the most comprehensive document up to now and confirmed our case–control findings.

Previous observational studies have reported inconclusive findings on the association between R/S and CVD. In a large national survey of the association between religious services attendance and CVD in the USA, higher service attendance was associated with a twofold lower risk of myocardial infarction in men, but not in women (OR = 0.50, 95% CI 0.26–0.97 in men; OR = 0.54, 95% CI 0.22–1.34 in women) (Obisesan et al. 2006). In a population-based case–control study from Albania, higher level of religious observance had protective effect on acute coronary syndrome both in Muslims and Christians (OR 0.48; 95% CI 0.31–0.74) (Burazeri et al. 2008). However, in the Women’s Health Initiative

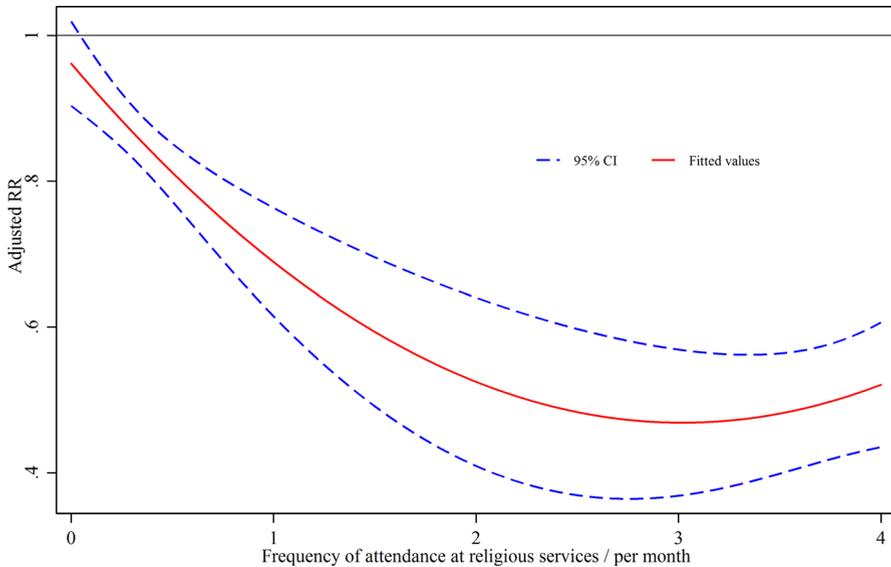


Fig. 2 Adjusted relative risk of coronary heart disease associated with frequency of attendance at religious services in a meta-analysis of observational studies. Religious services attendance was modeled using restricted cubic splines in a random-effect dose–response meta-analysis model. The value of zero (no services attendance) was considered as reference category. Solid line represents fitted value, dashed line represents 95% confidence interval, and solid horizontal line in the value of 1 indicates reference category (relative risk = 1). Horizontal axis indicates frequency of attendance at religious services per month, and vertical axis indicates adjusted relative risk

Observational Study in the USA, with 43,708 older women followed for 5 years, those with daily religious practice at baseline had higher adjusted risk of subsequent heart disease (HR = 1.21, 95% CI 1.01–1.45), while the risk for those attending less than once per week was not significant (HR 1.06; 95% CI 0.86–1.31) (Salmoirago-Blotcher et al. 2013). In the US National Heart, Lung, and Blood Institute’s Multi-Ethnic Study of Atherosclerosis (MESA), where participants were followed for 4.1 years, there was no association between daily, weekly, and monthly religious participation and subclinical CVD (Feinstein et al. 2010). The latest results from a prospective study of 74,534 women in the US Nurses’ Health Study were found a graded dose–effect reduction in mortality from CVD with increasing religious attendance, but the result was not significant for CHD (Li et al. 2016). Possible explanations for these conflicting findings are the ethnic diversity of populations under study, substantial age variation, different instruments for measurement of R/S, and variation in the concept of R/S in different cultures (Christian vs. Muslim) (as suggested by our meta-analysis, which showed substantial heterogeneity in the pooled analysis).

Our case–control study supports the hypothesis that elevated R/S is associated with lower odds of CHD among Muslims in a sample of Iranian population. The pooled result from our meta-analysis was consistent with this finding, and showed a trend toward a protective effect. One unanticipated finding was that in subgroup analysis based on design, pooled RR from case–control studies showed a negative association, but this result was in opposite direction in prospective cohort studies, which showed R/S as a possible risk factor for CHD. This may be because of the fact that the case–control studies are more

susceptible to various types of recall bias, especially because of retrospective nature of data collection (Parr et al. 2009). The potential effect of recall bias was measured in other fields of study such as cancer research (Parr et al. 2009), although to our knowledge there are no studies reporting this issue in R/S field. Therefore, the effect of recall bias in the field of R/S might be addressed in future studies. Also, another more likely explanation for this controversial result is less precision of secondary data analysis of large cohort studies. Indeed, smaller case–control studies with specific aims can devote more attention to accurate measurement of both exposure variable and possible confounders than large cohort studies with large number of variables and aims (Phillips and Smith 1993). None of the four cohorts in this meta-analysis was designed specifically for studying the association between R/S and CVD, and all of the four papers were secondary analysis of cohort data mainly designed for different purposes.

Strengths and Limitations

The present study has several strengths, including the matching of cases and controls, the multivariate analysis adjusting for well-known confounders, the assessment of a dose–response relationship and the detailed measurement of three dimensions of R/S (97 questions). Furthermore, in order to place our study results in the context of existing research, a meta-analysis was conducted that combined observational data from 238,100 individuals and 9709 CHD cases.

However, the present study also has several limitations that affect the interpretation and generalizability of the results. The best type of sampling method in case–control studies is population-based sampling, but we used hospital-based sampling method. Because when a person gets seriously sick, this may lead to a false elevation in religiosity attitude. For management of this potential phenomenon/bias, we selected the control group from hospitalized patient to compensate this false increase in exposure variable. The control group was selected maximally from patients with trauma, car accident, and under surgery for non-cancer- and non-cardiovascular-related diseases. Another limitation is potential effect of unknown residual confounders. But, for addressing this issue, we measured all the well-known confounders and controlled their effect using regression model. However, due to the fact that this is an observational study, we could not adjust for all possible psychological and social variables such as personality (A or B type), level of depression and anxiety, or social support, which could affect these relationships.

Conclusion

The present case–control study showed a dose–response association between increased level of R/S and lower odds of CHD. The results were consistent with pooled findings from other case–control studies, although not with four prospective cohort studies in Christian populations in the USA. Overall, we conclude that R/S confers a protective effect on CHD in Muslim adults living in Iran. Because of observational nature of the present study, we cannot conclude whether this association is casual. Prospective cohort studies and clinical trial studies that specifically designed to assess the effect of R/S on physical health outcome will be required to replicate these results and determine the direction of causation in this association.

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Compliance with ethical standards

Conflict of interest No conflict of interest for declaration.

Ethical approval The methodology and questionnaire of the present study were approved by central ethic committee of the Ilam University of Medical Sciences.

References

- Banerjee, A. T., Boyle, M. H., Anand, S. S., Strachan, P. H., & Oremus, M. (2014). The relationship between religious service attendance and coronary heart disease and related risk factors in Saskatchewan, Canada. *Journal of Religion and Health*, 53(1), 141–156. <https://doi.org/10.1007/s10943-012-9609-6>.
- Burazeri, G., Goda, A., & Kark, J. D. (2008). Religious observance and acute coronary syndrome in predominantly Muslim Albania: a population-based case-control study in Tirana. *Annals of Epidemiology*, 18(12), 937–945. <https://doi.org/10.1016/j.annepidem.2008.09.001>.
- Das, A., & Nairn, S. (2016). Religious attendance and physiological problems in late life. *Journals of Gerontology. Series B, Psychological Sciences and Social Sciences*, 71(2), 291–308. <https://doi.org/10.1093/geronb/gbu089>.
- Feinstein, M., Liu, K., Ning, H., Fitchett, G., & Lloyd-Jones, D. M. (2010). Burden of cardiovascular risk factors, subclinical atherosclerosis, and incident cardiovascular events across dimensions of religiosity: The multi-ethnic study of atherosclerosis. *Circulation*, 121(5), 659–666. <https://doi.org/10.1161/CIRCULATIONAHA.109.879973>.
- Friedlander, Y., Kark, J. D., & Stein, Y. (1986). Religious orthodoxy and myocardial infarction in Jerusalem—a case control study. *International Journal of Cardiology*, 10(1), 33–41.
- Go, A. S., Mozaffarian, D., Roger, V. L., Benjamin, E. J., Berry, J. D., Blaha, M. J., et al. (2014). Heart disease and stroke statistics—2014 update: A report from the American Heart Association. *Circulation*, 129(3), e28–e292. <https://doi.org/10.1161/01.cir.0000441139.02102.80>.
- Greenland, S., & Longnecker, M. P. (1992). Methods for trend estimation from summarized dose–response data, with applications to meta-analysis. *American Journal of Epidemiology*, 135(11), 1301–1309.
- Harbord, R. M., & Higgins, J. P. T. (2008). Meta-regression in Stata. *Stata Journal*, 8(4), 493–519.
- Higgins, J. P., & Thompson, S. G. (2004). Controlling the risk of spurious findings from meta-regression. *Statistics in Medicine*, 23(11), 1663–1682. <https://doi.org/10.1002/sim.1752>.
- Ikedo, F., Gangahar, D. M., Quader, M. A., & Smith, L. M. (2007). The effects of prayer, relaxation technique during general anesthesia on recovery outcomes following cardiac surgery. *Complementary Therapies in Clinical Practice*, 13(2), 85–94. <https://doi.org/10.1016/j.ctcp.2006.10.004>.
- Khodayarifard, M., & Rahiminejad, A. (2009). Preparation of religiosity scale and different levels of religiosity for Iranian society. Retrieved from <http://psyedu.ut.ac.ir/acstaff/khodayarifard/Research/Rf19.pdf>.
- King, D. E., Mainous, A. G., 3rd, & Pearson, W. S. (2002). C-reactive protein, diabetes, and attendance at religious services. *Diabetes Care*, 25(7), 1172–1176.
- Koenig, H. G. (2012). Religion, spirituality, and health: The research and clinical implications. *ISRN Psychiatry*, 2012, 278730. <https://doi.org/10.5402/2012/278730>.
- Ladwig, K. H., Lederbogen, F., Albus, C., Angermann, C., Borggrefe, M., Fischer, D., et al. (2014). Position paper on the importance of psychosocial factors in cardiology: Update 2013. *Ger Med Sci*, 12, Doc09. <https://doi.org/10.3205/000194>.

- Li, S., Stampfer, M. J., Williams, D. R., & VanderWeele, T. J. (2016). Association of religious service attendance with mortality among women. *JAMA Internal Medicine*, 176(6), 777–785. <https://doi.org/10.1001/jamainternmed.2016.1615>.
- Lucchese, F. A., & Koenig, H. G. (2013). Religion, spirituality and cardiovascular disease: Research, clinical implications, and opportunities in Brazil. *Revista Brasileira de Cirurgia Cardiovascular*, 28(1), 103–128. <https://doi.org/10.5935/1678-9741.20130015>.
- Nabel, E. G., & Braunwald, E. (2012). A tale of coronary artery disease and myocardial infarction. *New England Journal of Medicine*, 366(1), 54–63. <https://doi.org/10.1056/NEJMr1112570>.
- Nazarzadeh, M., Sarokhani, M., & Sayehmiri, K. (2015). The relationship between religious attitudes, fear of death and dying with general health condition: A survey in college students. *Journal of Religion and Health*, 54(5), 1672–1680. <https://doi.org/10.1007/s10943-014-9903-6>.
- Obisesan, T., Livingston, I., Trulear, H. D., & Gillum, F. (2006). Frequency of attendance at religious services, cardiovascular disease, metabolic risk factors and dietary intake in Americans: An age-stratified exploratory analysis. *International Journal of Psychiatry in Medicine*, 36(4), 435–448.
- Orsini, N., Bellocco, R., & Greenland, S. (2006). Generalized least squares for trend estimation of summarized dose–response data. *Stata Journal*, 6(1), 40–57.
- Orsini, N., & Greenland, S. (2011). A procedure to tabulate and plot results after flexible modeling of a quantitative covariate. *Stata Journal*, 11(1), 1–29.
- Parr, C. L., Hjartaker, A., Laake, P., Lund, E., & Veierod, M. B. (2009). Recall bias in melanoma risk factors and measurement error effects: A nested case-control study within the Norwegian Women and Cancer Study. *American Journal of Epidemiology*, 169(3), 257–266. <https://doi.org/10.1093/aje/kwn363>.
- Phillips, A. N., & Smith, G. D. (1993). The design of prospective epidemiological studies: More subjects or better measurements? *Journal of Clinical Epidemiology*, 46(10), 1203–1211.
- Powell, L. H., Shahabi, L., & Thoresen, C. E. (2003). Religion and spirituality. Linkages to physical health. *American Psychologist*, 58(1), 36–52.
- Ross, R. (1999). Atherosclerosis—an inflammatory disease. *New England Journal of Medicine*, 340(2), 115–126. <https://doi.org/10.1056/NEJM199901143400207>.
- Salmoirago-Blotcher, E., Fitchett, G., Hovey, K. M., Schnall, E., Thomson, C., Andrews, C. A., et al. (2013). Frequency of private spiritual activity and cardiovascular risk in postmenopausal women: The Women’s Health Initiative. *Annals of Epidemiology*, 23(5), 239–245. <https://doi.org/10.1016/j.annepidem.2013.03.002>.
- Schnall, E., Wassertheil-Smoller, S., Swencionis, C., Zemon, V., Tinker, L., O’Sullivan, M. J., et al. (2010). The relationship between religion and cardiovascular outcomes and all-cause mortality in the Women’s Health Initiative Observational Study. *Psychology and Health*, 25(2), 249–263. <https://doi.org/10.1080/08870440802311322>.
- Vandenbroucke, J. P., & Pearce, N. (2012). Case-control studies: Basic concepts. *International Journal of Epidemiology*, 41(5), 1480–1489. <https://doi.org/10.1093/ije/dys147>.
- Yates, J. S., Mustian, K. M., Morrow, G. R., Gillies, L. J., Padmanaban, D., Atkins, J. N., et al. (2005). Prevalence of complementary and alternative medicine use in cancer patients during treatment. *Supportive Care in Cancer*, 13(10), 806–811. <https://doi.org/10.1007/s00520-004-0770-7>.

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