

A longitudinal comparative analysis of economic and family caregiver burden due to bipolar disorder

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Abstract

Objective: to explain comparatively how economic and family caregiver burden in families with bipolar disorder patients change overtime. **Method:** one year follow-up of economic and family caregiver burden was carried out on family caregivers of 190 bipolar, 55 diabetes, hypertension and asthma patients and 659 sick controls in the community. Population average generalized estimating equation was used to make longitudinal comparative analysis. **Results:** bipolar patient family caregivers were found to be more burdened, for about 8 to 10 months of the year of study, than family caregivers of diabetes, hypertension and asthma and sick controls in the community. The average difference in family caregiver burden score between bipolar and diabetes, hypertension and asthma patient family caregivers was 4.36 ($z = -8.75, P > |z| = 0.001$); while the difference due to time between the two groups was 3.42 ($z = -4.27, P > |z| = 0.001$). Similarly, the average difference in family caregiver burden score between family caregivers of bipolar patient and sick controls in the community was 3.7 ($z = -4.88, P > |z| = 0.001$). In terms of longitudinal caregiver burden difference, bipolar patients family caregivers were found to be more burdened than family caregivers of sick controls in the community with a burden score difference of 2.97 ($z = -5.17, P > |z| = 0.001$). **Conclusion:** more should be done to lessen the economic and family caregiver burden due to bipolar disorder.

Key words: Bipolar disorder; Burden; Caregiver; Family

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Introduction

Bipolar disorder, characterized by recurrent manic and depressive or mixed episodes, is one of the most burdensome illnesses occurring in the early productive years of life.¹⁻⁷ Studies from Europe, America and Australia have found the economic burden of bipolar disorder to be substantially high.^{2-5,8,9} Bipolar disorder follows a chronic course and is associated with significant distress, disability, marital problems and premature mortality.^{10,11} Abuse of alcohol, drug and other substances is common, as well as an increased risk of co-morbid medical conditions. Patients with bipolar disorder tend

to have high demand for health services and yet the disorder is under-diagnosed and often inappropriately treated.¹²⁻¹⁶

Morbidity due to the recurrent nature of the illness, often exacerbated by co-existing medical conditions, has an undoubtedly large economic impact on individuals with the illness, their families, the health system and wider society. For example, it is known that family caregivers of bipolar patients have an increased use of health services themselves.¹⁷ Manic episodes of the illness are very disruptive to daily life, work and family relationships.¹⁸ During the acute phase of the illness great demand may be placed on family members to be involved in care giving. Such demands may persist even during remission, where residual symptoms may still be present demanding family care giving.^{18,19}

Bipolar disorder has direct and indirect costs resulting in economic and family caregiver burden. Cross sectional studies and data base analyses have shown this burden.^{2-6,8,9} However, little is known about how the economic and family

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caregiver burden in families with bipolar disorder patients changes over time. Furthermore, almost all studies of the economic and caregiver burden of bipolar disorder have been conducted in high-income countries. In low-income countries, families already living in poverty may be disproportionately affected by having a family member with bipolar disorder, in spite of the strong support networks existing in traditional societies. This paper presents the results of a one year follow-up study from rural Ethiopia comparing the economic and caregiver burden for families of patients with bipolar disorder to families of patients with other physical disorders. In addition, this paper reports on the pattern of burden over time.

Methods

Study subjects

The study was undertaken in Meskan and Mareko Wereda, a rural district in southern Ethiopia. In this district a course and outcome study project on bipolar disorder has been underway since the early 1990s. The project had screened all 83,282 adult population of the district for bipolar disorder by house to house survey using the WHO Composite International Diagnostic Interview (CIDI), Version 2.1.²⁰ The present study used a prospective longitudinal design involving all identified families with bipolar disorder patients. Two control groups of families were selected from follow-up clinics and from the community. The first control group included all families of follow-up attendees for diabetes, hypertension and asthma (DHA) in health institutions of the district and the second control group was composed of randomly chosen families from the community. From each group of families, family caregivers were selected using the method followed by Perlick et al. in their caregiver burden study.²¹

Thus, caregivers were selected based on the following criteria:

- is a spouse, parent or spouse equivalent to the patient;
- has most frequent contact with the patient;
- helps to support the patient financially;
- has most frequently been a collateral in the patient's treatment; and
- is contacted by treatment staff in case of emergency.

To be included in the sample as a caregiver, the chosen caregiver had to satisfy at least three of the criteria.

Consequently, this study sampled all 190 families of bipolar patients who were under follow-up during the survey, the first control group of 55 families with DHA patients (35 diabetes mellitus, 12 hypertension and 8 asthmatics), and the second control group of 659 randomly selected families in the community. The total sample size of the study comprised of 904 families of caregivers.

During data collection from families of controls from the community, a family member was considered as a caregiver if any other illness had affected a family member and care had been rendered to the ill person by other family member(s). Therefore, in each of the groups, illness was defined as having an individual family member whose normal functioning was interrupted due to a health problem.

Data collection

The data collection was carried out every two months for one year, which commenced in July 2004 and ended in June 2005.

Data collection instruments were developed and pre-tested three times in a nearby community. The purpose of these repeated pre-tests was to increase the reliability and validity of interview instruments. Accordingly, interview instruments with a reliability test coefficient less than 0.40 were dropped. In each of the pre-testing sessions, one week of extensive training was provided for data collectors and supervisors. Using the refined final interview instruments, data was collected on economic and family caregiver burden. Data quality and consistency cross-checks were made by another group of trained supervisors recruited for the purpose. For data entry EpiInfo 6 version 6.04d statistical software was used while SPSS 11.0 and Stata/SE 8.2 for Windows were used for data analysis.

Burden measurement

Longitudinal burden measurements were made using out-of-pocket medical expenses for health services, time lost due to care giving and the extent of family caregiver burden. Out-of-pocket medical expenses included cost of: travel, medical examination, drugs and injections, laboratory service, food and accommodation; the time lost due to care giving included time lost in accompanying patient to and from health institutes and lost days of work due to care giving at home. There were 15 questionnaire items constituting family caregiver burden, with response categories on a five-point scale (Table I). During each interview, family caregivers were asked about the extent of burden they had experienced in the month prior to interview using the 15 questionnaire items. Thus, family burden score of 1 to 5 was given based on the frequency of occurrence of a 'burden-causing event': 1 = did not happen at all in the month; 2 = happened at least once per week in the month; 3 = happened at least twice per week in the month; 4 = happened at least 3 to 6 times per week in the month; and 5 = happened almost every day per week in the month.

Table I. Questionnaire items constituting family caregiver burden, Butajira-Ethiopia, 2005

To what extent the:

- patients illness causes sleep disturbance,
- patient's illness creates burden on job,
- patient's illness limits social relation movement,
- patient's illness creates burden as to ignore other family members,
- patient's illness creates feeling of unhappiness,
- patient's illness creates worry about the future,
- to what extent were you ashamed due to the patient's illness,
- when you think about the patient, to what extent you feel guilty,
- how much do you worry by saying that I am unable to cope-up more than this,
- to what extent patient's illness create health problem,
- to what extent your relationship with the patient was in crisis due to the patient's illness,
- to what extent the patient causes physical injury on you,
- to what extent life was problematic and challenging for you due to the patient's illness,
- to what extent the patient's illness creates burden on you as to think of suicide, and
- to what extent were you happy about patient's social relationships?

Analysis

Longitudinal economic and family caregiver burden comparisons of caring for bipolar patients were made using two arms of control. The first arm was family caregivers of DHA patients and the second arm was family caregivers of sick controls in the community (SCC). Chi-square and t-test were used to compare socio-demographic characteristics. Descriptive mean comparisons were made in terms of out-of-pocket medical expenses for health services, time lost due to care giving and the extent of family caregiver burden. From time one (baseline) through six (end of the study); family caregiver burden was computed as the respondent's average responses across the 15 items constituting family caregiver burden. Finally, a population average generalized estimating equation was used to explain the change over time in family caregiver burden. For the purpose of comparison all costs were converted to US\$ by using the mean exchange rate for 2005 of Ethiopian currency (Birr 8.6810 = 1US\$).²² The study was ethically approved by the Faculty of Medicine Addis Ababa University and oral informed consent to participate in the study was obtained from the study subjects.

Results

Out of the 190 eligible families with a member suffering from bipolar disorder, 26 were inaccessible, six had changed address, six were unavailable, four refused, two died and seven did not have caregivers, leaving 139 participating family caregivers. From the first control group of 55 families with DHA

patients; 12 had changed address, two were unavailable, one refused and four did not have family caregivers, leaving 36 participating families. From the second control group of 659 randomly selected families with sick controls in the community, 472 families participated but only 402 had family caregivers (one also refused). From this group, 146 had changed address and the status of 18 subjects was unknown. Therefore, family caregivers of 139 bipolar patients, 36 DHA (diabetes, hypertension, and asthma) patients and 401 SCC (sick controls in the community) were involved in the final study. The majority of participants were female, married and non-literate (Table II). The mean monthly living expenses of bipolar patient family caregivers was \$9.28 (SD = \$8.44) while that of DHA and SCC family caregivers was \$19.70 (SD= \$12.16) and \$3.41 (SD= \$5.64) respectively. Likewise, mean annual family income of bipolar patient family caregivers was \$154.72 (sd= \$178.77) while the mean annual family income of DHA patient and SCC family caregivers was \$417.64 (sd= \$330.22) and \$57.01 (sd= \$107.73) respectively. Caregivers were found to be comparable in their socio-demographic characteristics, however, some differences were observed between bipolar and DHA patients in terms of other educational level and occupations. These differences were accounted for in further analyses.

During the year, bipolar patient family caregivers had the highest mean out-of-pocket medical expenses (\$93.93) compared to DHA patient (\$64.80) and SCC family caregivers (\$56.18). The expense borne by bipolar patient family caregivers ranged from \$6.62 (median= \$4.38) to \$30.55

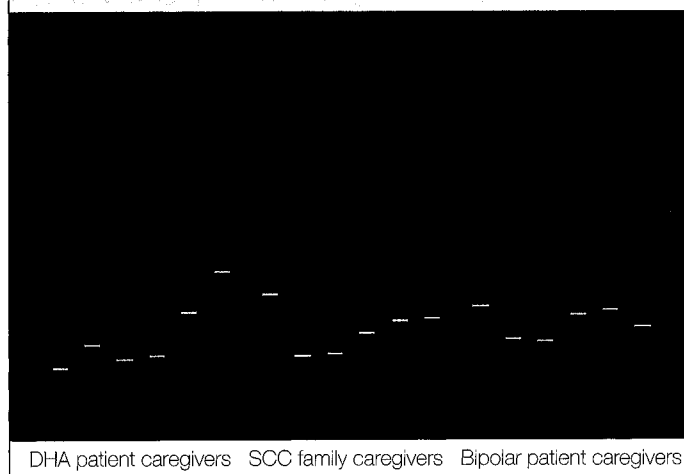
Table II. Sociodemographic characteristics of family caregivers, Butajira-Ethiopia, 2005.

Variable	Bipolar patient family caregivers N=139, (%)	DHA patient family caregivers N=36, (%)	SCC family caregivers N=401, (%)
Sex	56 (40.29)	12(33.33)	163(40.65)
Male	83 (59.71)	24(66.67)	238(59.35)
Female			
Age mean(sd)	37.58 (13.87)	37.47(14.76)	34.06(11.96)
Family size mean(sd)	6.23 (2.54)	7.08(3.05)	5.64(2.08)
Marital status			
Married	112 (80.58)	27(75.00)	328(81.80)
Others	27 (19.42)	9(25.00)	73(18.20)
Educational level			
Illiterate	90(64.75)	12(33.33)	256(63.84)
Literate	41(29.50)	12(33.33)	122(30.42)
Others	8(5.75)	12(33.33)	23(5.74)
Occupation			
Farmer	49(35.25)	8(22.22)	136(33.92)
Housewife	65(46.76)	11(30.56)	199(49.63)
Merchant	11(7.91)	6(16.66)	17(4.24)
Other	14(5.76)	11(30.56)	49(12.21)
Relation with the family			
Household head/Father	48(34.53)	8(22.22)	139(34.66)
Mother	70(50.36)	20(55.56)	199(49.62)
Child	12(8.63)	7(19.44)	52(12.96)
Brother/Sister	8(5.76)	-	8(1.99)
Other	1(0.72)	1(2.78)	4(0.99)
Religion			
Orthodox	37(26.62)	18(50.00)	104(25.94)
Islam	90(64.75)	13(36.11)	266(66.99)
Protestant	12(8.63)	5(13.89)	31(7.73)

(median= \$2.88) per month. Family caregiver comparisons in terms of lost days of work due to care giving in one month revealed that, on average, bipolar patient family caregivers lost 1.78 days (sd = 4.54) while DHA patient and SCC family caregivers lost 2.66 (sd = 5.78) and 2.32 days (sd = 5.02) respectively. However, these differences in mean out-of-pocket medical expense and lost days of work among caregivers were not statistically significant.

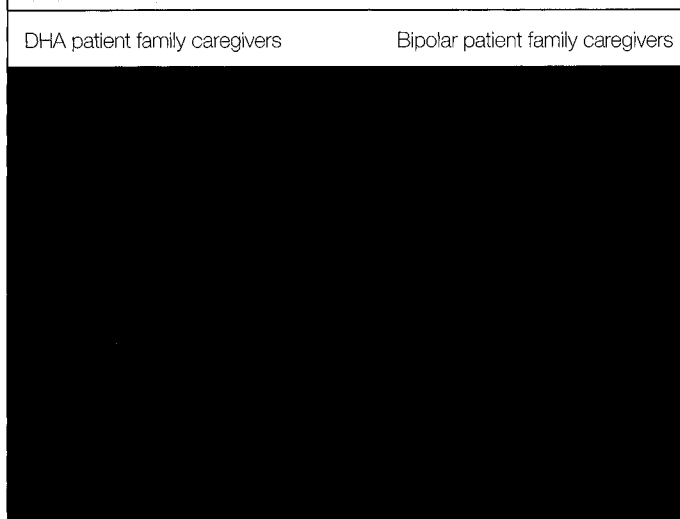
Longitudinal comparative analysis of family caregiver burden between bipolar and DHA patient family caregivers, using the respondent's average responses across the 15 items, found that the median scores of bipolar patient family caregiver burden were at the higher side of the scale for about 10 months (from time one to five), compared to the median family caregiver burden scores of DHA patient family caregivers (Figure 1). It was only at time six that median family caregiver burden scores of DHA patient family caregivers exceeded the median scores of bipolar patient family caregivers. Similar comparison of bipolar and SCC family caregivers also revealed that the median family caregiver burden scores of bipolar patient family caregivers were higher for about 8 months (from time two through five). However, at times one and six the median family caregiver burden scores of SCC family caregivers were on the higher side. But overall, bipolar patient family caregivers were on the higher side of the scores signifying that bipolar patient family caregivers were more burdened than DHA patient and SCC family caregivers.

Fig 1. Box plots of family caregiver burden for six follow-up periods, Butajira-Ethiopia, 2005.



Mean and standard error plot comparisons of family caregiver burden between bipolar and DHA patient family caregivers showed that mean family caregiver burden scores of bipolar patient family caregivers were on the higher side of the scale from time 1 through 4, that is, for about 8 months, than mean family caregiver burden scores of DHA patient family caregivers (Figure 2). The mean difference in family caregiver burden between bipolar and DHA patient family caregivers was statistically significant ($t = -2.23, P > |t| = 0.03, 95\%CI= 0.70, 0.84$). However, more variability was observed in DHA patient family caregivers particularly from time three to six.

Fig 2. Family caregiver burden mean and standard error plots for bipolar and DHA patient family caregivers, Butajira-Ethiopia, 2005.



A similar result was obtained from mean and standard error plot comparisons of family caregiver burden between bipolar and SCC family caregivers. Bipolar patient family caregivers had higher mean burden scores from time two to five, again for about 8 months, than SCC family caregivers (Figure 3). Also this mean difference in family caregiver burden between bipolar patient family caregivers and SCC family caregivers was statistically significant ($t = -13.39, P > |t| = 0.0001, 95\%CI= 0.34, 0.41$). Again in these mean and standard error plot comparisons it was demonstrated that bipolar patient family caregivers had been more burdened than DHA patients and SCC family caregivers. In general, the median burden score analyses and the mean and standard error plot comparisons showed that across the total 12 month period of the study, bipolar patient family caregivers were more burdened for about 8 to 10 months when compared to DHA patient and SCC family caregivers.

Further analysis of family caregiver burden using a population average generalized estimating equation with

Fig 3. Family caregiver burden mean and standard error plots for bipolar patient and SCC family caregivers, Butajira-Ethiopia, 2005.

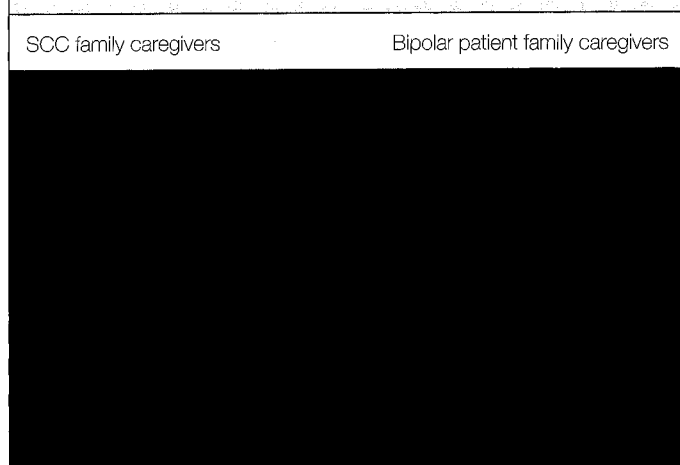


Table III. Population average generalized estimating equation analysis of family caregiver burden between bipolar and DHA patient family caregivers, Butajira-Ethiopia, 2005.

GEE population-averaged model		Number of obs = 144				
Group and time vars: subject time		Number of groups = 44				
Link:	identity	Obs per group: min = 2				
Family:	Gaussian	avg = 3.3				
Correlation:	AR(1)	max = 6				
Scale parameter: 0.2043554		Wald chi2(9) = 810.55				
		Prob > chi2 = 0.0000				
(standard errors adjusted for clustering on subject)						
Caregiver burden Coef.		Semi-robust Std. Err.	z	P> z	[95% Conf. Interval]	
Caregiver	-1.25	0.14	-8.75	0.000	-1.54 -0.97	
Time	-0.29	0.07	-4.27	0.000	-0.43 -0.16	
Sex	-0.01	0.06	-0.24	0.809	-0.12 0.09	
Age	-0.01	0.00	-2.33	0.020	-0.01 -0.00	
Marital status	-0.05	0.06	-0.73	0.464	-0.18 0.08	
Educational level	-0.01	0.06	-0.12	0.903	-0.13 0.11	
Occupation	0.01	0.06	0.27	0.789	-0.09 0.12	
Family size	-0.00	0.03	-0.25	0.803	-0.04 0.03	
Interaction	0.21	0.02	13.46	0.000	0.18 0.24	
Constant	13.11	0.24	13.17	0.000	2.65 3.58	
Estimated within-subject correlation matrix R:						
	c1	c2	c3	c4	c5	c6
r1	1.0000					
r2	0.1914	1.0000				
r3	0.0366	0.1914	1.0000			
r4	0.0070	0.0366	0.1914	1.0000		
r5	0.0013	0.0070	0.0366	0.1914	1.0000	
r6	0.0003	0.0013	0.0070	0.0366	0.1914	1.0000

autoregressive working correlation (Table III) demonstrated that the average difference in family caregiver burden score between bipolar and DHA patient family caregivers was 4.36 ($z = -8.75$, $P > |z| = 0.001$). It was also shown that the difference due to time between the two group of family caregivers was 3.42 ($z = -4.27$, $P > |z| = 0.001$). In addition, it was also found that the interaction among the variables of being a family caregiver of bipolar patients, caregiver burden and time was statistically significant with a caregiver burden score difference of 3.32 ($z = 13.46$, $P > |z| = 0.001$).

Similarly when comparing bipolar patient family caregivers with SCC family caregivers (Table IV), the average family caregiver burden score difference was 3.7 ($z = -4.88$, $P > |z| = 0.001$). In terms of longitudinal caregiver burden difference, bipolar patients family caregivers were found to be more burdened than SCC family caregivers with a burden score difference of 2.97 ($z = -5.17$, $P > |z| = 0.001$). Besides, the interaction among the variables of being a family caregiver of bipolar patient, caregiver burden and time was statistically significant with a caregiver burden score difference of 2.88 ($z = 16.14$, $P > |z| = 0.001$), signifying that when considered longitudinally, care-giving for bipolar patients was more burdensome than care-giving for sick controls in the community (SCC).

In summary, this study found that the economic and family

caregiver burden due to bipolar disorder was greater for families with bipolar disorder patients than the economic and family caregiver burden of families with diabetes, hypertension and asthma patients or families with sick controls at the community.

Discussion

To the best of our knowledge, this is the first study which has comparatively explored how family caregiver burden due to bipolar disorder changes over time. In this study, bipolar patient family caregivers were found to be burdened above the median score for about two thirds of the year. Caregiver burden score differences between family caregivers of bipolar patients and the two comparison groups revealed that a burden causing event happened at least three to six times per week in the months of the year on family caregivers of bipolar patients, whereas on family caregivers of DHA patients and SCC, burden causing events had not happened in most of the months of the year. In addition, compared to DHA patients and SCC family caregivers, the burden experienced by family caregivers of bipolar disorder patients was for a longer period of time. The longitudinal time change of burden experienced by family caregivers of bipolar disorder patients was significantly different from the longitudinal time change of burden experienced by family caregivers of DHA patients and SCC. In this longitudinal time change of burden, family

Table IV. Population average generalized estimating equation analysis of family caregiver burden between bipolar patient family caregivers and SCC family caregivers, Butajira-Ethiopia, 2005.

GEE population-averaged model		Number of obs = 141				
Group and time vars: subject time		Number of groups = 47				
Link:	identity	Obs per group: min = 2				
Family:	Gaussian	avg = 3.0				
Correlation:	AR(1)	max = 6				
Scale parameter: .1760814		Wald chi2(9) = 835.77				
		Prob > chi2 = 0.0000				
(standard errors adjusted for clustering on subject)						
Caregiver burden Coef.		Semi-robust Std. Err.	z		P> z	[95% Conf. Interval]
Caregiver	-1.03	0.21	-4.88	0.000	-1.44	-0.61
Time	-0.30	0.06	-5.17	0.000	-0.41	-0.19
Sex	0.05	0.09	0.55	0.581	-0.13	0.23
Age	-0.00	0.00	-1.12	0.262	-0.01	0.00
Marital status	0.00	0.09	0.03	0.972	-0.18	0.18
Educational level	-0.06	0.10	-0.59	0.553	-0.26	0.14
Occupation	0.04	0.07	0.60	0.549	-0.09	0.17
Family size	-0.01	0.02	-0.52	0.604	-0.04	0.02
Interaction	0.21	0.01	16.14	0.000	0.19	0.24
Constant	2.67	0.33	7.99	0.000	2.01	3.32
Estimated within-subject correlation matrix R:						
	c1	c2	c3	c4	c5	c6
r1	1.0000					
r2	0.2866	1.0000				
r3	0.0821	0.2866	1.0000			
r4	0.0235	0.0821	0.2866	1.0000		
r5	0.0067	0.0235	0.0821	0.2866	1.0000	
r6	0.0019	0.0067	0.0235	0.0821	0.2866	1.0000

caregivers of bipolar patients were found to be more burdened than DHA patients and SCC family caregivers. Moreover, money and time of family caregivers of bipolar disorder patients had been directly and indirectly taxed. They had spent their money for their bipolar relatives seeking medical help and had also lost days of work due to care giving, although not significantly more than the comparison groups.

With regard to the extent of burden, our findings were consistent with findings of other studies.²³⁻²⁷ A longitudinal hospital based study in the US, involving caregivers of bipolar disorder patients, reported that over 90 percent of family caregivers had experienced at least moderate levels of burden whereas over 50 percent of the caregivers had experienced severe levels.²³ Another South American cross-sectional study reported high levels of burden in relatives of people with schizophrenia.²⁴ In another study from Nigeria, rural families of schizophrenics were reported to shoulder a heavy burden of treatment and transportation for follow-up.²⁵ The five European centers study on relatives of patients with schizophrenia had also reported that relatives experience high level of burden, spending 7 to 9 hours daily with the patient.²⁶

As in the South American study our findings also revealed that there was no difference in family care giving burden due to age or marital status. Also, like the European centers study the majority of the caregivers in our study were females.

However, in our study there was no family caregiver burden difference between male and female family caregivers. Furthermore, our findings showed that there was no difference in family caregiver burden due to differences in occupation, marital status and educational level among the study subjects. This might be due to similarities among study subjects which might indicate inadequate representativeness of the sample. Moreover, lack of difference in terms of educational level, as usually expected, may also mean that caregivers understanding of patients' condition were also similar or this may need to be further explored to establish the cultural norm of defining caregiver burden in the study population. Even though, our findings were consistent (in some respect) with the aforementioned studies, there were methodological differences. In some of the studies family caregivers were assessed clinically so as to know the influence of patients' clinical status on caregivers' burden. They also used different interview instruments and analytic methods.

In the current study, care giving was more burdensome for bipolar patient family caregivers. With time, these caregivers may become overburdened as the longitudinal change in family burden score was persistent for most months of the year. In this regard a previous study has reported that patients living with an overburdened caregiver may have increased risk of relapse, therefore, attention should be given to the bipolar's patient family caregivers.²¹ In addition, the annual

cost of out-of-pocket medical expense (\$93.93) made by family caregivers of bipolar patients was substantially higher than the out-of-pocket medical expense made by DHA patient and SCC family caregivers. If we consider this out-of-pocket medical expense at societal level, by taking into consideration one percent life time prevalence as a lower margin and the average 2.9 percent life time prevalence of different studies done at different times in urban and rural Ethiopia as a higher margin; and assuming that each case of bipolar disorder had at least one family caregiver, then the total direct cost to the Ethiopian society was approximately between \$39.1 to \$113 million.²⁸⁻³³ Likewise, the indirect cost of loss of working days due to care giving (by assuming \$0.92 as a wage for a day's work) was approximately between \$5.4 to \$15.5 million. Therefore in 2005, the total economic burden of family care giving for patients with bipolar disorder in Ethiopia ranged approximately between \$45.5 million to \$128.5 million. Compared to other studies in the western world, the total economic burden of care giving for bipolar disorder patients seems minimal.^{2-4,8} But, for a low income developing country like Ethiopia, this is huge. Of course these cost estimates involve a lot of approximation because of uncertainty involved in the calculation. However, it is undeniable that the figures give an insight into how burdensome family care giving is for bipolar disorder patients in a low income developing country.

Conclusion

Generally more should be done in the direction of lessening the economic and family caregiver burden due to bipolar disorders. Health policy and priority setting need to be attuned in accordance with the available evidence of burden from bipolar disorder and other mental health problems. Family caregivers should be supported through family and follow-up clinic based educational programs. Caregivers who can cope better with patients' behavior or who can improve their coping abilities over time experience less burden.³⁴ Future studies need to focus more on how to devise feasible intervention strategies to lessen economic and family caregiver burden due to bipolar disorder and also need to define cultural norms of care giving in the study community. Finally, the study has been undertaken longitudinally; and it is among the first that described the economic and family caregiver burden of caring for bipolar disorder patients at the community level. However, direct comparison of the results of the study with other studies conducted elsewhere was limited. Also, the sample may not be adequately representative, so the results of the study should be cautiously interpreted.

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Declaration of relative contribution

Ababi Zergaw, the first author of this article is a doctoral candidate who was responsible for the conception, design, analysis and interpretation of the study data. He was the principal investigator who had run the overall research

process. He drafted and revised the article producing the final form for publication. He had collected original data, thus, he had full access to all the data in the study, and was responsible for the integrity of the data and the accuracy of the data analysis.

Damen Hailemariam, MD, MPH, Ph.D. was the first advisor of the candidate. He had contributed in the designing stage of the study and critical review of the manuscript. He approved the final version of the article for publication.

Atalay Alem, MD, Ph.D. was the second advisor of the candidate. He had contributed in the designing stage of the study and critical review of the manuscript.

Derege Kebede, MD, MSc. Sc.D. was the third advisor of the candidate. He had contributed in the designing stage of the study and critical review of the manuscript.

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