

What is already known on this topic

Amoxicillin is effective in treating non-severe pneumonia in children

Isolation of infective bacteria from the nasopharynx can be used to monitor antimicrobial resistance in the community

What this study adds

Three days of treatment with amoxicillin is as effective as the standard five days in treating non-severe pneumonia

Almost three quarters of nasopharyngeal isolates of *Streptococcus pneumoniae* and *Haemophilus influenzae* were resistant to co-trimoxazole

biological advantages in the selection process. This phenomenon results in the use of one class of antibiotics promoting carriage of *S pneumoniae* resistant to another antibiotic class.⁹

Conclusions

A three day course of amoxicillin for treating community acquired non-severe pneumonia in children, is equally effective as a five day course but is cheaper with increased adherence and possibly decreased emergence of antimicrobial resistance. Our findings have local as well as global implications, because our study

has also confirmed findings from a recently published data from elsewhere.

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Risk factors, prevalence, and treatment of anxiety and depressive disorders in Pakistan: systematic review

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Abstract

Objectives To assess the available evidence on the prevalence, aetiology, treatment, and prevention of anxiety and depressive disorders in Pakistan.

Design Systematic review of published literature.

Studies reviewed 20 studies, of which 17 gave prevalence estimates and 11 discussed risk factors.

Main outcome measures Prevalence of anxiety and depressive disorders, risk factors, effects of treatment.

Results Factors positively associated with anxiety and depressive disorders were female sex, middle age, low level of education, financial difficulty, being a housewife, and relationship problems. Arguments with husbands and relational problems with in-laws were positively associated in 3/11 studies. Those who had close confiding relationships were less likely to have anxiety and depressive disorders. Mean overall prevalence of anxiety and depressive disorders in the community population was 34% (range 29-66% for women and 10-33% for men). There were no rigorously controlled trials of treatments for these disorders.

Conclusions Available evidence suggests a major social cause for anxiety and depressive disorders in Pakistan. This evidence is limited because of methodological problems, so caution must be exercised in generalising this to the whole of the population of Pakistan.

Introduction

Anxiety and depressive disorders constitute a substantial proportion of the global burden of disease, and are projected to form the second most common cause of disability by 2020.¹ Non-communicable diseases such as these present a particular challenge for low income countries, where infectious diseases and malnutrition are still rife, and where only a low percentage of gross domestic product is allocated to health services.² These

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References w1-w20 are listed on bmj.com



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disorders are also important because of their economic consequences.³

With an estimated population of 152 million, Pakistan is the sixth most populous country in the world, and is projected to be the fourth most populous by 2050.⁴ There is a need to develop an evidence base to aid policy development on tackling anxiety and depressive disorders. We therefore conducted a systematic review as no such work existed to our knowledge.

Our main questions were (a) what the estimated prevalence of anxiety and depressive disorders is in Pakistan and how this compares with estimates from other low income countries; (b) what the associated social, psychological, and biological factors are; and (c) what evidence exists for effectiveness of treatment or prevention in this population.

Methods

Data sources

Using the key words "Pakistan" and ("mental" or "depression" or "anxiety" or "psychiatric"), we searched bibliographic databases, reference lists of retrieved articles, Pakmedinet.com, and the *Pakistan Journal of Clinical Psychiatry* until 1995, when it ceased publication. See bmj.com for details.

Study selection

We selected studies that were conducted within Pakistan and that focused on depression, depressive disorder, or anxiety disorder in adults (ages 18-65). We assessed the methodological quality of the selected studies, but since relatively few addressed our study questions, we included all studies directly relevant to the questions regardless of their quality. A narrative synthesis of the extracted studies was performed to address the questions of the review.

Results

We found 20 studies that directly addressed the questions of the review: 19 were cross sectional epidemiological surveys, and one was a case-control study.^{w1-w20} Seventeen gave prevalence estimates (n=9170), while 11 discussed associated risk factors. We did not find any prospective study of the natural course of the disorder or a rigorously controlled study of any interventions. We found little qualitative work. Sample sizes ranged from 113 to 2620 in prevalence studies (mean 539.41, median 298).

Methods of included studies

Only three of the 11 prevalence studies published in local journals gave adequate details of methods. Because of this, it is difficult to comment on possible biases. Diagnoses in all the studies were made by either a psychiatrist or a trained worker using a validated instrument, and thus seem to be of reasonably good quality.

Most of the studies discussed the generalisability of their findings but did not interpret any null findings. In the discussions, national comparisons were rarely made with findings of other national research groups; comparisons were usually with studies in other countries.

Prevalence of anxiety and depressive disorders

The overall mean prevalence in men and women in the six studies of random community samples (n=2658) was 33.62%, with the point prevalence varying from 28.8% to 66% for women (overall mean 45.5%) and from 10% to 33% for men (overall mean 21.7%). Women aged 15-49 were studied in a paper with 28.8% prevalence, while young men with a mean age of 18 participated in a study reporting 33% prevalence. Only one study reported adjusted prevalence with 95% confidence intervals.

Factors associated with risk of anxiety and depressive disorders in studies included in systematic review

| Study | Negative association | Positive association | No association |
|-------------------------------------|---|---|--|
| Population based sample: | | | |
| Hussain et al 2000 ^{w7} | Higher level of education | Women; unemployment; widowed, separated, or divorced; ≥4 children; loss of a child or father during childhood; marked independent chronic difficulties (housing, financial, health) | |
| Mumford et al 1996 ^{w13} | Higher level of education, higher socioeconomic status | | Life events, joint or nuclear family |
| Mumford et al 1997 ^{w14} | General wealth factor, higher level of education in younger men and women | Age, women living in unitary households | |
| Mumford et al 2000 ^{w15} | Higher level of education especially in young women, higher socioeconomic variables in women | Age, women living in joint households, | |
| Rabbani et al 2000 ^{w18} | Husband employed | Older women, longer duration of marriage, arguments with husband or in-laws, lack of autonomy | Disturbing event in family (P=0.08) |
| Primary care sample: | | | |
| Ali et al 1993 ^{w1} | | Women, housewives | Income (P=0.06) |
| Ali et al 2000 ^{w2} | Higher level of education | Women, young adults and late middle age group, married | |
| Dodani et al 2000 ^{w4} | Higher level of education | More than 12 members in a single household | Marriage |
| Secondary and tertiary care sample: | | | |
| Bender 2001 ^{w3} | | Social problems, relational problems with in-laws compared with other social problems | |
| Case-control study: | | | |
| Naeem 1992 ^{w16} | | Absence of confiding relationship with husband | Loss of mother before age 11, ≥3 children under age of 14 at home, lack of paid employment |
| Qualitative study: | | | |
| Rabbani 1999 ^{w17} | Social support from talking with husband, health care provider, friends, or religious leaders | Perceived factors: low family income, marital disputes, verbal abuse by in-laws, too many children | |

For those presenting to traditional or faith healers (n = 511), the prevalence of anxiety and depressive disorders among men varied from 2.65% to 27%, and among women from 11.5% to 52%.

Three studies looked at total psychiatric morbidity in primary care (n = 774). One described women in a rural area, with a prevalence of 50%, while another described 18% prevalence for men and 42.2% for women in an urban area. The third study, with a prevalence of 38.4%, did not specify participants' sex.

Of those presenting to psychiatric outpatients (n = 2430), the prevalence varied between 32% and 66.3%. There were two studies on psychiatric inpatients, one reported a prevalence of depressive illness of 37% (n = 2620), while the other reported 19.1% (n = 177).

Associated social, psychological, and biological factors

The table shows the various factors found to be associated with anxiety and depressive disorders. Increased prevalence was associated with female sex, middle age, low level of education, difficulties with finances, being a housewife and relationship problems.

What is the evidence for effectiveness of treatment or prevention in this population?

We could not find any prospective study of the natural course of the disorder or any rigorous controlled study addressing effectiveness of treatment and prevention. We found only one randomised controlled trial in mental health, regarding the ability of schoolchildren to detect mental disorders after having been given health education.⁵

Discussion

In our systematic review we found that socioeconomic adversity and relationship problems were major risk factors for anxiety and depressive disorders in Pakistan, whereas supportive family and friends may protect against development of these disorders.

Limitations of study

Our review may be subject to publication and selection bias as we were unable to systematically contact the experts in Pakistan for unpublished material or grey literature.

The coverage of the studies we identified is low. Most studies satisfying our inclusion criteria were from the provinces of Punjab and Sindh, the two provinces with the largest population. The epidemiological data were collected from a handful of villages and urban settlements. There was considerable methodological variation in study design and in the instruments used. Thus one is unable to extrapolate these epidemiological findings to the whole of Pakistan.

Comparison with other low income countries

Using stringent criteria, Harding et al reported an overall frequency of anxiety and depression of 13.9% in four developing countries.⁶ Community studies from Africa have reported prevalences of 24% in rural Uganda and 20%-24% in rural South Africa. Among patients attending primary care, the prevalence varied from 8% to 29%. Patients attending primary care in India showed prevalences between 21% and 57%.⁷

What is already known on this subject

Anxiety and depressive disorders are associated with considerable economic burden

These disorders represent an emerging public health threat in low income countries

What this study adds

In Pakistan relationship problems, financial difficulties, and low educational level are positively associated with anxiety and depressive disorders, whereas having a supportive relationship is negatively associated

Systematically collected, peer reviewed evidence suggests an overall prevalence of 34% for anxiety and depressive disorders in this population, but this finding must be treated with caution because of methodological limitations

Nationally representative psychiatric morbidity surveys and controlled treatment trials are needed to inform policy in order to control morbidity from anxiety and depressive disorders in Pakistan

In relation to risk factors, Abas and Broadhead found a significant association with formal employment, below average income, overcrowding, and certificate of secondary education in urban Zimbabwe.⁸ In the same study, they also found a significant association with humiliation or entrapment and with death or other loss.⁹ Bhagwanjee in rural South Africa found similar risk factors to those from Pakistan.¹⁰ However, we found that the reported overall rates were higher in Pakistan and higher among rural than urban populations compared with the above studies. The question is whether these differences are an artefact of measurement or are because of specific factors operating in Pakistan.

Pakistan's population has been exposed to sociopolitical instability, economic uncertainty, violence, regional conflict, and dislocation for at least the past three decades.¹¹ These are risk factors for psychiatric disorders² and may help explain the findings of this review.

The need for stronger evidence and improved research capacity

A coherent mental health policy with a strategic implementation plan is essential for countries that wish to enhance their social, economic, and social capital.¹²

A major obstacle in formulating effective health policy is the lack of robust epidemiological research in Pakistan.¹³ The time is right for Pakistan to build on this research effort, increase investment in research capacity and develop a national epidemiological survey of mental disorders.

Conclusion

Available evidence suggests a major social cause for anxiety and depressive disorders in Pakistan, and an overall prevalence of 34%. This evidence is limited because of methodological problems. Nationally representative psychiatric morbidity surveys and controlled treatment trials are required to inform

policy in order to control morbidity from anxiety and depressive disorders.

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Randomised, controlled trial of ginkgo biloba and acetazolamide for prevention of acute mountain sickness: the prevention of high altitude illness trial (PHAIT)

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Abstract

Objective To evaluate the efficacy of ginkgo biloba, acetazolamide, and their combination as prophylaxis against acute mountain sickness.

Design Prospective, double blind, randomised, placebo controlled trial.

Setting Approach to Mount Everest base camp in the Nepal Himalayas at 4280 m or 4358 m and study end point at 4928 m during October and November 2002.

Participants 614 healthy western trekkers (487 completed the trial) assigned to receive ginkgo, acetazolamide, combined acetazolamide and ginkgo, or placebo, initially taking at least three or four doses before continued ascent.

Main outcome measures Incidence measured by Lake Louise acute mountain sickness score ≥ 3 with headache and one other symptom. Secondary outcome measures included blood oxygen content, severity of syndrome (Lake Louise scores ≥ 5), incidence of headache, and severity of headache.

Results Ginkgo was not significantly different from placebo for any outcome; however participants in the acetazolamide group showed significant levels of protection. The incidence of acute mountain sickness was 34% for placebo, 12% for acetazolamide (odds ratio 3.76, 95% confidence interval 1.91 to 7.39, number needed to treat 4), 35% for ginkgo (0.95, 0.56 to 1.62), and 14% for combined ginkgo and acetazolamide (3.04, 1.62 to 5.69). The proportion of patients with increased severity of acute mountain sickness was 18% for placebo, 3% for acetazolamide

(6.46, 2.15 to 19.40, number needed to treat 7), 18% for ginkgo (1, 0.52 to 1.90), and 7% for combined ginkgo and acetazolamide (2.95, 1.30 to 6.70).

Conclusions When compared with placebo, ginkgo is not effective at preventing acute mountain sickness. Acetazolamide 250 mg twice daily afforded robust protection against symptoms of acute mountain sickness.

Introduction

Acute mountain sickness occurs above 2000 m secondary to failed physiological adaptation to acute hypobaric hypoxia. This rapidly reversible condition is characterised by headache, lightheadedness, fatigue, nausea, and insomnia. Although primary risk factors, such as ascent rate and exertion, can be modified, pharmaceutical prevention with acetazolamide is also effective despite side effects that may reduce compliance.

Ginkgo biloba, an antioxidant herbal supplement, has emerged as a prophylactic agent for the prevention of acute mountain sickness.¹⁻⁶ Indirect evidence suggests that it may prevent hypoxic damage in tissues, and in clinical trials its side effects were similar to placebo.^{7,8} Results from these small randomised controlled trials have, however, been mixed.

We compared the effect of ginkgo, acetazolamide, or combined ginkgo and acetazolamide with placebo on

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