Knowledge of Neural Tube Defects and Prevention Through Folic Acid Use Among Women in Faisalabad, Punjab, Pakistan: A Cross-Sectional Survey

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Objective: Neural tube defects (NTDs) are one of the most common congenital abnormalities of the central nervous system and are associated with significant mortality, morbidity, and major life-long disability. Periconceptional folic acid reduces the risk of NTDs by up to 70%; however, in Pakistan, no public information program exists concerning the risks of NTDs or promoting folic acid use. As such, the aim of this study was to assess levels of knowledge about NTDs and folic acid use among women attending the gynaecology department of DHQ Hospital, Faisalabad, Pakistan.

Design: A cross-sectional survey.

Setting: The gynaecology department of the District Head Quarter (DHQ) Hospital in Faisalabad, Pakistan.

Participants: Three hundred and fifty-five married women.

Primary and Secondary Outcome Measures: Primary outcome measures included knowledge of NTDs and knowledge of folic acid use.

Results: About 85.4% of participants had no knowledge of neural tube defects and 76.7% reported no knowledge about folic acid use. The majority of participants (86.2%) were unaware that folic acid protects against NTDs. Lack of knowledge of NTDs was significantly associated with education (P = 0.001), husband’s education (P = 0.002), planned pregnancy (P = 0.002), sources of antenatal care (P = 0.003), knowledge of folic acid (P = 0.003), knowledge that folic acid protects against NTDs (P = 0.002), and health decision-making (P = 0.003). Knowledge of folic acid use was significantly associated with age (P = 0.000), education (P = 0.004), husband’s education (P = 0.002), monthly income (P = 0.003), planned pregnancy (P = 0.003), pregnancy trimester (P < 0.001), sources of antenatal care (P < 0.001), knowledge of NTDs (P = 0.002), knowledge that folic acid protects against NTDs (P < 0.001), use of folic acid (P < 0.001), sources of vitamin information (P < 0.001), and health decision-making (P = 0.002).

Conclusion: These findings highlight extremely low levels of knowledge about NTDs and folic acid use of women in Pakistan. There is an urgent need to increase knowledge and awareness of the risks of NTDs and preventative approaches, through health education programs delivered by trusted health professionals.

Keywords: neural tube defects, folic acid, knowledge, health education

Introduction

Neural tube defects (NTDs) are serious birth defects that affect the brain and spinal cord. NTDs develop in early pregnancy (between 21 to 28 days gestation) due to a failure of the neural tube to close and form the embryonic central nervous system.¹ These brain and spinal cord conditions are the most common neurological defects in neonates and children with lifelong disabilities, including lower limb paralysis, incontinence, hydrocephalus, and intellectual and learning disabilities.¹ NTDs include spina bifida, anencephaly, encephalocele and craniorachiasis, which vary in severity.²
NTDs have a global prevalence of 0.3 to 1.99 per 1000 live births.\textsuperscript{3} However, the prevalence of NTDs varies according to region, ranging from 9.0 cases per 10,000 live births in the European region, to 21.9 cases in the Eastern Mediterranean region.\textsuperscript{3} NTDs are associated with significant mortality, morbidity, and major life-long disability, yet evidence suggests a simple dietary supplement of folic acid (a synthetic form of vitamin B) may prevent up to 75% of all cases, when 400mcg is taken daily throughout the periconceptional period.\textsuperscript{4–9}

As such, countries such as the United States, Canada, Costa Rica, South Africa, and Chile have effectively implemented food fortification with folic acid added to enriched grain products. This has resulted in significant decreases in NTDs to as low as five to six cases per 10,000 pregnancies.\textsuperscript{10,11} Educational interventions have also been implemented in parts of China and the USA, the findings of which have showed significant improvements in knowledge about the use of folic acid.\textsuperscript{12–14}

However, such policies and interventions have not been implemented globally and in many developing countries knowledge and use of folic acid, as well as awareness of NTDs is low.\textsuperscript{15,16} For example, a recent study conducted in Ethiopia found that over 90% of mothers had no knowledge of folic acid use, including mothers of NTD affected babies. Further to this, 100% of the mothers surveyed were unaware of NTDs and the link with folic acid.\textsuperscript{17} Prevalence of NTDs, especially in developing countries, is showing an increasing trend, with NTDs responsible for 29% of neonatal deaths that are due to noticeable birth defects in low-income countries.\textsuperscript{18–20}

In Pakistan, NTDs are a serious, preventable public health issue, as women lack knowledge about folic acid\textsuperscript{15} and, contrary to Government legislation and foreign aid initiatives (eg from UK DfID, US Aid and other NGOs), fortified foods have not been made available.\textsuperscript{21} No formal data is available for the prevalence of NTDs in Pakistan,\textsuperscript{22} however some studies have estimated prevalence to be between 12 to 14 cases per 1000 live births,\textsuperscript{23,24} or between 38.6 to 124.1 per 10,000 live births,\textsuperscript{3} which far surpasses rates recorded in Western nations.

A plethora of factors affecting use of vitamins or supplements in Pakistan have been reported in the literature. These include limited antenatal facilities, lack of knowledge about the benefits, lack of availability, cost, resistance from family members, fear of side-effects, and misconceptions about the nature of the supplement.\textsuperscript{25} Many of these barriers relate to a lack of understanding about the nature and purpose of folic acid. It is therefore crucial that public knowledge and education about the benefits of periconceptional folic acid use is improved. In order to do this, it is first necessary to assess current levels of knowledge and understanding about NTDs and folic acid use of women in Pakistan.

The aims of this study are to 1) assess levels of knowledge about NTDs and 2) assess levels of knowledge about folic acid use.

**Methods**

**Study Design and Setting**

This study was part of a British Council funded collaboration between the Faculty of Social Sciences, at the University of Agriculture in Faisalabad, Pakistan, and the School of Social Sciences, at the University of Manchester in the UK. The research was carried out at the District Head Quarter (DHQ) Hospital in Faisalabad, Pakistan.

Recruitment took place in the gynaecology ward of the hospital from June to September 2015. A cross-sectional study was used to collect quantitative data.

**Sample and Recruitment**

Women were purposively sampled using a non-probability technique. Both pregnant and non-pregnant women of childbearing age (18 to 45 years) were eligible to participate. Participants were invited to take part in the study by members of the research team who informed them of the study and obtained informed consent for the survey. These women were attending hospital for pregnancy-related, infertility, and contraception medical check-ups and treatments either before, during, or after pregnancy. Women who agreed to participate were asked to complete the survey on the same day. Around 10% of women asked to participate refused due to anxiety about inclusion in the study.
Data Collection
Data were collected using a questionnaire administered by the research team, coordinated by the lead researcher (SY). The questionnaire was pre-tested and corrected to verify the validity of the questions. The questionnaire comprised three sections; the first section gathered information about the socio-economic status of respondents including age, education levels of the participants and their husbands, employment of the participants and their husbands, and monthly family income. The second section gathered data on whether participants were currently pregnant, pregnancy planning, and pregnancy trimester, number of living children, miscarriage history, source of antenatal care and how health decisions were made in the family. The third section assessed knowledge of NTDs, folic acid, folic acid to protect against NTDs, use of folic acid, and preferred delivery method of information about vitamins and supplements to improve maternal and foetal health. Women were questioned about attitudes and practices of their husbands, as husbands usually have a role in decision-making where women are seeking healthcare, particularly related to pregnancies and contraception.

Data Analysis
Data were analysed using SPSS v22.0. Descriptive statistics were calculated to characterise distributions of different variables and responses. Chi-square tests were used to examine levels of knowledge about NTDs and folic acid use. Results with two tailed $P$ values $<0.05$ were considered statistically significant.

Patient and Public Engagement
No patient involved.

Results
Participant characteristics, pregnancy history, and bivariate associations are presented in Table 1.

Participant Characteristics
A total of 355 women participated in the study. Most participants were aged between 26 to 30 years old and had no formal education. The majority of participants were unemployed and the majority of participants’ husbands were employed in manual labour jobs and most had no formal education. For the majority of participants, their monthly family income was below 5000 rupees (around £49.38 or $68.20).

Pregnancy History
At the time of completing the survey, the majority of participants were not pregnant and had at least one living child. Of those who were pregnant, the majority were in their third trimester. 57.7% of participants reported that their last pregnancy was planned and 30.4% of participants reported having miscarried their previous pregnancy. With regards to antenatal visits, most participants reported receiving care from a nurse. Most participants reported that their husband was responsible for making decisions about medical visits.

Knowledge About NTDs and Folic Acid
The majority of participants reporting having no knowledge of NTDs or folic acid. Accordingly, the majority of participants reported not knowing that folic acid reduces the risk of NTDs and did not use folic acid during pregnancy. With regards to desired sources of information about vitamins and use, the majority of participants reported that they would like to receive this information through their doctor.

Bivariate Associations
A significant association was found between lack of knowledge of NTDs and education ($P=0.001$), husband’s education ($P=0.002$), planned pregnancy ($P=0.002$), sources of antenatal care ($P=0.003$), knowledge of folic acid ($P=0.003$), knowledge that folic acid reduces the risk of NTDs ($P=0.002$), and health decision making in the family ($P=0.003$).
|                | Total | Knowledge of NTDs | Knowledge of Folic Acid |
|----------------|-------|-------------------|-------------------------|
|                | n= 355 (%) | Yes (n) | No (n) | Not Sure (n) | P-value | Yes (n) | No (n) | Not Sure (n) | P-value |
| Age            |       | 34 | 303 | 18 | 0.676 | 69 | 258 | 28 | <0.001 |
| 41–45          |       | 11 (3.1) |       |       |       |       |       |       |       |
| 36–40          |       | 23 (6.5) |       |       |       |       |       |       |       |
| 31–35          |       | 40 (11.3) |       |       |       |       |       |       |       |
| 26–30          |       | 153 (43.0) |       |       |       |       |       |       |       |
| 21–25          |       | 101 (28.5) |       |       |       |       |       |       |       |
| 15–20          |       | 27 (7.6) |       |       |       |       |       |       |       |
| Employment status |       |       |       |       | 0.08 |       |       |       | 0.075 |
| Employed       |       | 52 (14.6) |       |       |       |       |       |       |       |
| Unemployed     |       | 303 (85.3) |       |       |       |       |       |       |       |
| Education levels |       |       |       |       | 0.001 |       |       |       | 0.004 |
| Graduate       |       | 18 (5.1) |       |       |       |       |       |       |       |
| A-level        |       | 22 (6.2) |       |       |       |       |       |       |       |
| GCSE           |       | 44 (12.4) |       |       |       |       |       |       |       |
| Middle         |       | 53 (14.9) |       |       |       |       |       |       |       |
| Primary education |       | 72 (20.3) |       |       |       |       |       |       |       |
| No formal education illiterate |       | 146 (41.1) |       |       |       |       |       |       |       |
| Husband's occupation |       |       |       |       | 0.402 |       |       |       | 0.004 |
| Government job |       | 11 (3.1) |       |       |       |       |       |       |       |
| Manual labour  |       | 217 (61.1) |       |       |       |       |       |       |       |
| Self-employed  |       | 101 (28.4) |       |       |       |       |       |       |       |
| Unemployed     |       | 26 (7.3) |       |       |       |       |       |       |       |
| Husband's education |       |       |       |       | 0.002 |       |       |       | 0.002 |
| Higher         |       | 16 (4.5) |       |       |       |       |       |       |       |
| A-level        |       | 21 (5.9) |       |       |       |       |       |       |       |
| GCSE           |       | 19 (5.4) |       |       |       |       |       |       |       |
| Middle         |       | 54 (15.2) |       |       |       |       |       |       |       |
| Primary education |       | 113 (31.8) |       |       |       |       |       |       |       |
| No formal education illiterate |       | 132 (37.2) |       |       |       |       |       |       |       |
| Monthly income (Rup) |       |       |       |       | 0.082 |       |       |       | 0.003 |
| 11,000–15,000  |       | 41 (11.5) |       |       |       |       |       |       |       |
| 5000–10,000    |       | 64 (18.0) |       |       |       |       |       |       |       |

(Continued)
| Health decisions       | Total | Knowledge of NTDs | Knowledge of Folic Acid |
|------------------------|-------|------------------|------------------------|
|                        | n = 355 (%) | Yes (n) | No (n) | Not Sure (n) | P-value | Yes (n) | No (n) | Not Sure (n) | P-value |
| < 5000                 | 221 (62.3) | 148 (67.0) | 46 (21.0) | 27 (12.0) | 0.003 | 29 (8.2) | 22 (47.9) | 205 (44.9) | 0.002 |
| No income              | 29 (8.2) | 16 (55.2) | 7 (24.1) | 6 (20.7) |       |       |       |       | |
| Planned pregnancy      |       |       |       |       |       |       |       |       |       |
| Only you               | 54 (15.2) | 39 (72.2) | 5 (9.2) | 10 (18.8) | 0.003 |       |       |       | 0.003 |
| Mainly Husband         | 154 (43.4) | 116 (75.5) | 23 (15.0) | 15 (9.5) | 0.002 |       |       |       | 0.003 |
| Joint Decision         | 65 (18.3) | 46 (70.8) | 7 (10.8) | 12 (18.5) |       |       |       |       |       |
| Other                  | 82 (23.1) | 55 (67.1) | 9 (11.0) | 8 (9.8) |       |       |       |       |       |
| Living children        |       |       |       |       |       |       |       |       |       |
| Yes                    | 307 (86.5) | 235 (76.8) | 38 (12.4) | 34 (11.0) | 0.047 |       |       |       | 0.227 |
| No                     | 48 (13.5) | 32 (66.6) | 6 (12.5) | 10 (20.8) |       |       |       |       |       |
| Planned pregnancy      |       |       |       |       |       |       |       |       |       |
| Yes                    | 205 (57.7) | 148 (72.5) | 20 (9.8) | 37 (18.7) | 0.003 |       |       |       | 0.003 |
| No                     | 150 (42.3) | 97 (64.7) | 25 (16.7) | 28 (18.7) |       |       |       |       |       |
| Currently pregnant     |       |       |       |       |       |       |       |       |       |
| Yes                    | 149 (41.9) | 106 (71.0) | 18 (12.1) | 25 (16.9) | 0.18  |       |       |       | 0.009 |
| No                     | 206 (58.1) | 138 (67.1) | 32 (15.9) | 36 (17.8) |       |       |       |       |       |
| Pregnancy trimester    |       |       |       |       |       |       |       |       |       |
| 1                      | 23 (6.4) | 18 (78.3) | 2 (8.7) | 1 (4.3) | 0.421 |       |       |       | <0.001 |
| 2                      | 41 (11.5) | 36 (87.8) | 2 (4.9) | 3 (7.3) |       |       |       |       |       |
| 3                      | 85 (23.9) | 75 (87.7) | 6 (7.1) | 4 (4.7) |       |       |       |       |       |
| Prior miscarriage      |       |       |       |       |       |       |       |       |       |
| Yes                    | 108 (30.4) | 88 (81.5) | 8 (7.4) | 12 (11.1) | 0.726 |       |       |       | 0.35  |
| No                     | 247 (69.6) | 164 (66.5) | 30 (12.0) | 53 (21.5) |       |       |       |       |       |
| Antenatal care         |       |       |       |       |       |       |       |       |       |
| Doctor                 | 66 (18.6) | 53 (80.3) | 4 (6.1) | 9 (13.6) | 0.003 |       |       |       | <0.001 |
| Nurse                  | 140 (39.4) | 119 (85.0) | 15 (10.7) | 6 (4.3) |       |       |       |       |       |
| Traditional birth attendants | 87 (24.5) | 73 (83.9) | 6 (6.9) | 8 (9.2) |       |       |       |       |       |
| Other                  | 62 (17.5) | 52 (83.9) | 6 (9.7) | 4 (6.4) |       |       |       |       |       |
| Knowledge of NTDs      |       |       |       |       |       |       |       |       |       |
| Yes                    | 34 (9.5) | 29 (85.3) | 4 (11.8) | 1 (2.9) | 0.002 |       |       |       |       |
| No                     | 303 (85.4) | 251 (82.9) | 40 (13.2) | 22 (7.4) |       |       |       |       |       |
| Not sure               | 18 (5.1) | 15 (83.3) | 2 (11.1) | 1 (5.6) |       |       |       |       |       |
A significant association was also found to exist between knowledge of folic acid and participants’ age ($P=0.001$), education ($P=0.004$), husband’s education ($P=0.002$), monthly income ($P=0.003$), planned pregnancy ($P=0.003$), pregnancy trimester ($P<0.001$), sources of antenatal care ($P<0.001$), knowledge of NTDs ($P=0.002$), knowledge that folic acid protects against NTDs ($P<0.001$), use of folic acid ($P<0.001$), sources of vitamin information ($P<0.001$), and health decision making in the family ($P=0.002$).

**Table 1** (Continued).

|                                | Total | Knowledge of NTDs | Knowledge of Folic Acid |
|--------------------------------|-------|-------------------|------------------------|
|                                | n= 355 (%) | Yes (n) | No (n) | Not Sure (n) | P-value | Yes (n) | No (n) | Not Sure (n) | P-value |
| Knowledge of folic acid        |       |          |        |            |         |          |        |            |         |
| Yes                            | 57 (16.0) |          |        |            | 0.003   |          |        |            |         |
| No                             | 272 (76.7) |          |        |            |         |          |        |            |         |
| Not sure                       | 26 (7.3) |          |        |            |         |          |        |            |         |
| Use of folic acid              |       |          |        |            | 0.512   |          |        |            | <0.001  |
| Yes                            | 69 (19.4) |          |        |            |         |          |        |            |         |
| No                             | 258 (72.7) |          |        |            |         |          |        |            |         |
| Not sure                       | 28 (7.9) |          |        |            |         |          |        |            |         |
| Folic acid decreases risk of NCDs |       |          |        |            | 0.002   |          |        |            | <0.001  |
| Yes                            | 29 (8.2) |          |        |            |         |          |        |            |         |
| No knowledge                   | 306 (86.2) |          |        |            |         |          |        |            |         |
| Not sure                       | 20 (5.6) |          |        |            |         |          |        |            |         |
| Sources of vitamin information |       |          |        |            | 0.512   |          |        |            | <0.001  |
| TV                             | 143 (40.3) |          |        |            |         |          |        |            |         |
| Doctor                         | 180 (50.7) |          |        |            |         |          |        |            |         |
| Other                          | 12 (3.2) |          |        |            |         |          |        |            |         |
| Not sure                       | 20 (5.6) |          |        |            |         |          |        |            |         |

A significant association was also found to exist between knowledge of folic acid and participants’ age ($P=0.001$), education ($P=0.004$), husband’s education ($P=0.002$), monthly income ($P=0.003$), planned pregnancy ($P=0.003$), pregnancy trimester ($P<0.001$), sources of antenatal care ($P<0.001$), knowledge of NTDs ($P=0.002$), knowledge that folic acid protects against NTDs ($P<0.001$), use of folic acid ($P<0.001$), sources of vitamin information ($P<0.001$), and health decision making in the family ($P=0.002$).

**Discussion**

The purpose of this study was to assess levels of knowledge about NTDs and folic acid use in women attending an urban health centre in Faisalabad, Pakistan. The findings reveal low levels of knowledge about both NTDs and folic acid use, which supports the findings of previous studies conducted in Pakistan$^{15,16}$ and elsewhere.$^{17,27}$

Our findings highlight the need to increase knowledge about both NTDs and the use of folic acid during the periconceptual period. Previous research has demonstrated the benefits of educational interventions on not only knowledge and awareness of folic acid use, but also on uptake; A US-based educational intervention was shown to increase awareness of folic acid from 78% to 98%, and knowledge about its role in preventing birth defects from 82% to 92%.$^{28}$ Furthermore, awareness campaigns have been shown to increase usage in the UK from 6% to 41%,$^{29}$ and from 8% to 35% (between 1992–2007) in the US.$^{30}$

The findings of these studies clearly demonstrate the effectiveness of educational interventions to improve knowledge and awareness of NTDs and folic acid use, and may be an effective approach to utilise in Pakistan. Based on our findings, trusted health professionals may be best placed to deliver health education to all women before they conceive. This is
a common finding across various antenatal contexts and settings. Previous research has reported a high level of interest and engagement from Pakistani women in the provision of health information, which suggests that educational interventions may be well received.

However, women whose pregnancies are unplanned may not benefit from this approach. It is therefore important for government bodies to implement fortification of food products with folic acid in addition to educational programmes. This approach in itself presents a major opportunity to reduce the risks of NTDs for at risk populations. Combining both approaches would therefore enhance risk reduction and ensure all pregnancies received some level of protection.

Our study findings also reveal high levels of unemployment and low levels of education and household income. In the majority of cases, decision-making surrounding health issues was made by the husband or another party (eg, mother-in-law). Furthermore, a significant association was found between the education levels of women and their husbands, and health decision-making, and knowledge of NTDs and folic acid use.

These findings are consistent with those of other studies in Pakistan and in other developing countries (eg) and highlights the problematic nature of women’s lack of autonomy and independence. Mumtaz et al, conducted a qualitative study exploring the social determinants of poor women’s access to maternal health services in Pakistan: despite national and community level interventions, on the basis of occupational hierarchy or caste system (the caste system is a form of social stratification based on family background). Women in marginalized groups were found to have no access to timely and basic maternal health care and were reported to be treated unfairly by government healthcare providers. This is important, as an absence of appropriate antenatal care, limited access to supplementation, and family members prohibiting the use of vitamins have been suggested to be the main contributors to high levels of NTDs in Pakistan.

The associations found between education levels and folic acid use lend support for the findings of previous studies. Higher levels of education have been shown to be positively related with knowledge of folic acid in different studies around the world (eg). This highlights the importance of providing an education program accessible to all to impart simple information about prevention of birth defects through supplementation and/or fortified foods or, at the very least, better diet and lifestyles. Given the association between education and use of preventatives, this strategy may work if delivered in the appropriate way for different parts of society.

In the present study, knowledge of NTDs and folic acid use were also significantly associated with pregnancy planning. These findings provide support for previous studies among Norwegian and Italian mothers in which maternal education and planned pregnancy were strong predictors of folic acid use. Conversely, high rates of unplanned pregnancy have been suggested to be the cause of low folic acid use in Turkey. This provides further confirmation that food fortification is an important approach to employ, to ensure that all women are provided with some level of protection against affected pregnancies.

There are several limitations to this study. This study was limited to one public hospital in Faisalabad and only included pregnant, presumed married women. This limits our ability to generalise to a wider population and to understand how representative the findings are within Pakistan. Future research would therefore benefit from recruiting a more representative sample, both in terms of setting and participant characteristics. Self-report measures were also used as the primary means of data collection. Whilst this method was appropriate for the study design, response biases may have affected the way in which participants responded to the survey items and is something that should be considered. Additionally, this study assessed associations between variables and outcome measures, but did not investigate the direction of these associations although these can be determined from Table 1. Future research would be well placed to explore these associations further in order to draw more firm conclusions about the nature of the interactions.

**Conclusion**

The findings of this study show extremely low levels of knowledge about NTDs, as well as low levels of knowledge about folic acid and the efficacy of this supplement to prevent devastating birth defects. There is an urgent need to address this public health issue by delivering health education through trusted health professionals and for government bodies to implement food fortification in an effective manner, to deliver fortified foods to all at risk populations.
Strengths and Limitations of This Study

- A cross-sectional survey was carried out to assess levels of knowledge about neural tube defects and folic acid use.
- A sample of 355 participants was recruited.
- Chi-squared tests were used to examine bivariate associations.
- Further analysis is required to determine the direction of significant associations.

Data Sharing Statement
All raw data and SPSS data files are available from the lead researcher (SY).

Ethics
The study complies with the Declaration of Helsinki on ethical principles for research involving human subjects. The study design, including the verbal informed consent process, was approved by the Office of Research, Innovation and Commercialization, at the University of Agriculture in Faisalabad, Pakistan, the management of the DHQ Hospital and their Research Ethics committee, and the University of Manchester Research Ethics Committee. Verbal informed consent was obtained from all participants, as most were illiterate, from poor rural areas, and unable to write their own names. However, all participants were informed about the purpose of the study and reassured that their personal information would remain confidential.

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Author Contributions
All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure
The authors declare no conflicts of interest for this work.

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