SCHISANHERBA paniculata Thunb. is a member of the family Rubiaceae and is indigenous to the mountainous regions of northern and south-eastern China (1). It is a perennial herb with slender, erect stems, and is commonly found in forests and along roadsides. The plant is known for its medicinal properties and is used in traditional Chinese medicine for various purposes.

The leaves of Schisandra paniculata are rich in various bioactive compounds, including triterpenoids, flavonoids, and lignans. These compounds have been implicated in a wide range of biological activities, including anti-inflammatory, antioxidant, and anti-cancer properties (2). In this study, we investigated the effects of aqueous extracts of Schisandra paniculata on the viability of HepG2 cells, a human hepatocellular carcinoma cell line.

Materials and Methods

Cell Culture

HepG2 cells were obtained from the American Type Culture Collection (ATCC, Manassas, VA) and grown in DMEM medium (Gibco, Grand Island, NY) supplemented with 10% fetal bovine serum (FBS) and penicillin/streptomycin (Gibco). The cells were maintained in a humidified atmosphere containing 5% CO₂ at 37°C.

Preparation of Aqueous Extract

Dry leaves of Schisandra paniculata were powdered and extracted with distilled water. The extracts were then filtered and concentrated under vacuum to obtain a crude aqueous extract. The concentration of the extract was determined using a spectrophotometer (Shimadzu UV-1800, Kyoto, Japan) at 280 nm.

Cell Viability Assay

HepG2 cells were seeded at a density of 5 x 10³ cells per well in 96-well plates. After 24 hours, the cells were treated with different concentrations of the aqueous extract (0.01-10 μg/mL) and incubated for 24 hours. Cell viability was measured using the MTT assay (3). The absorbance was read at 570 nm using a microplate reader (Bio-Tek Instruments, Winooski, VT).

Results

The results showed a dose-dependent inhibition of cell viability in HepG2 cells treated with the aqueous extract of Schisandra paniculata. The IC₅₀ (concentration that inhibits 50% of cell viability) was calculated to be 1.25 μg/mL. The extract also induced apoptosis in HepG2 cells, as indicated by an increase in the percentage of Annexin V-positive cells.

Conclusion

The aqueous extract of Schisandra paniculata exhibited cytotoxic activity against HepG2 cells. This study provides evidence for the antiproliferative and apoptotic effects of the extract, which may be attributed to its bioactive constituents. Further studies are needed to elucidate the molecular mechanisms underlying these effects.

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lead to poor quality of life and holistic approach by the physician may be helpful in managing these problems in addition to underlying RA symptomatology.\textsuperscript{9} 
Rheumatoid arthritis has not been an uncommon disease in our setup. Every year a lot of patients get diagnosed and put on medications for this chronic multisystem disease. A lot of work has been done on clinical and laboratory aspects of this disorder, but we lack holistic approach towards it both from clinical and research point of view. A recent study done on women with arthritis in Lahore concluded that significant correlation exists between depression, anxiety and sexual dysfunction among women with arthritis. They also highlighted the importance of psychological treatment along with the medical treatment for the women with arthritis.\textsuperscript{10} We therefore planned and conducted this study with the rationale to determine the sexual dysfunction among the patients of rheumatoid arthritis and assess the relationship of various factors with presence of sexual dysfunction.

**METHODOLOGY**

This cross-sectional was conducted at rheumatology department of Pak Emirates Military Hospital (PEMH) Rawalpindi, from August 2019 and April 2020. Sample size was calculated by using the WHO sample size calculator and keeping the population prevalence proportion at 66.8%.\textsuperscript{11} Screening was performed on rheumatology outpatient department of PEMH Rawalpindi who fulfilled the American College of rheumatology classification criteria of RA\textsuperscript{12} with age between 18-45 years were included in this study. Non probability consecutive sampling technique was used to gather the required sample size for this study. Patients who had unclear diagnosis or those with RA as part of other broad immunological condition were excluded from the study. Patients with psychological or sexual problems prior to onset of RA (checked by detailed history taking) were also excluded from the study. Patients with recent surgeries of any kind or suffering from any sort of gynecological infections were also excluded from the study. Presence of polycystic ovarian disease or any other endocrine problem was also part of the exclusion criteria. Patients with mastectomy or colostomy were also excluded from the study.

Female sexual function index (FSFI) was the validated tool used to study the sexual function among females in our study. For then on - English understanding patients validated Urdu translation was used.\textsuperscript{13} A global sum of “26” or less indicates the sexual dysfunction.\textsuperscript{14}

Patients were provided with a detailed description of the study and were inducted into the study after written informed consent. Ethics approval with IREB letter no A/124 was obtained before the start of the study. Confounding variables like presence of chronic physical or mental illness or gynecological infection or sexual problems prior to the diagnosis of RA were identified by detailed history taking and excluded from the study. The FSFI questionnaire was administered to the women and were asked to answer the questions according to their condition in last two weeks. Socio demographic variables were also collected. Variables in the study included age, duration of RA, Use of polypharmacy (use of more than one drugs to control RA) and medical comorbidities other than exclusion criteria (DM, HTN, Asthma, IHD).

Statistical analysis for this study was performed using Statistics Package for Social Sciences version 24. Characteristics of participants and the distribution of the FSFI score were described by using the descriptive statistics. Participants were resulted by categorical compared by normal sexual function v/s sexual dysfunction. Chi-square test was done to evaluate factors related to sexual dysfunction and extent of the relationship in the target population. Differences between groups were considered significant if p-values were less than or equal to 0.05.

**RESULTS**

A total of 350 married women with RA were included in the study after the application of inclusion/exclusion criteria. Mean age of the study participants was 31.15 ± 4.22 years. Mean duration of illness was 3.58 ± 1.297 years. Out of these 350 women suffering

**Table-I: Characteristics of patients included in the study.**

| Factors                     | Values          |
|-----------------------------|-----------------|
| Age (years)                 | 31.15 ± 4.217   |
| Range (min-max)             | 19 - 44 years   |
| Mean duration of illness    | 3.58 ± 1.297    |
| Presence of Sexual Dysfunction |                 |
| Yes                         | 178 (50.9%)     |
| No                          | 172 (49.1%)     |
| Polypharmacy                |                 |
| Yes                         | 123 (35.2%)     |
| No                          | 227 (64.8%)     |
| Presence of Comorbidities   |                 |
| No                          | 280 (80%)       |
| Yes                         | 70 (20%)        |
from rheumatoid arthritis screened through FSFI, 172 (49.1%) had normal sexual function while 178 (50.9%) had sexual dysfunction. Table-I shows general characteristics of study participants. Table-II shows that after applying the chi-square test, polypharmacy and long duration of illness held this strong association with sexual dysfunction (p-value <0.05) while age and presence of comorbidities had no statistically significant relationship with the dependent variable in the study.

Table-II: Pearson chi-square analysis: Factors related to sexual dysfunction among the women suffering from rheumatoid arthritis.

| Factors                  | Subjects with normal sexual function | Subjects with sexual dysfunction | p-value |
|--------------------------|--------------------------------------|---------------------------------|---------|
| Age                      |                                      |                                 |         |
| ≤35 year                 | 149 (86.7%)                          | 146 (82.1%)                     | 0.236   |
| >35 year                 | 23 (13.3%)                           | 32 (17.9%)                      |         |
| Presence of Comorbidities|                                      |                                 |         |
| No                       | 133 (77.3%)                          | 147 (82.2%)                     | 0.219   |
| Yes                      | 39 (22.7%)                           | 31 (17.8%)                      |         |
| Polypharmacy             |                                      |                                 |         |
| No                       | 122 (70.9%)                          | 105 (58.9%)                     | 0.019   |
| Yes                      | 50 (29.1%)                           | 73 (41.1%)                      |         |
| Duration of Illness      |                                      |                                 |         |
| <5 years                 | 103 (59.8%)                          | 71 (39.9%)                      | <0.001  |
| ≥5 years                 | 69 (40.2%)                           | 107 (60.1%)                     |         |

**DISCUSSION**

Physiological functions of the body like eating sleeping and sexual function may alter in any chronic medical condition either due to pathophysiology of condition or medications used or psychosocial aspects of the illness. Traditionally used biomedical model only focused on limited aspects of the disease but holistic model covers all the dimensions of illness and focus on overall quality of life of an individual. Rheumatoid arthritis has been one of the most commonly encountered immune based inflammatory conditions which almost affect all he systems of the body\textsuperscript{15}. Sexual function has physiological, psychological and endocrine basis which may get altered either with immune based process of RA or the medication used. We planned this study with the rationale to determine the sexual dysfunction among the patients of rheumatoid arthritis and assess the relationship of various factors with presence of sexual dysfunction among the target population.

Boone et al in 2019 published a study with objective to look for the presence of sexual problems among female patients suffering from rheumatoid arthritis, psoriatic arthritis (PsA) and health controls. They concluded that though a high percentage of healthy controls (44%) suffered from sexual dysfunction as well but this problem was significantly found more among patients with rheumatoid and psoriatic arthritis. Disease activity in both diseases was associated with presence and severity of sexual dysfunction. Sexual dysfunction also emerged as predictor of poor health related quality of life among patients of both types of arthritis included in the study\textsuperscript{16}. We did not include patients of psoriatic arthritis and studies health related quality of life but regarding RA our results were quite comparable with the results of Boone et al as a huge percentage of our study participants had sexual problems.

A study from Tunisia published in 2019 by Alia et al evaluated sex related problem among females suffering from RA in Tunisia in case-control design. Patients with RA had almost double the prevalence of sexual problems as compared to the healthy controls. They studied individual components of sexual cycle and female sexual function index and almost all the items were affected more in patients of RA as compared to the controls\textsuperscript{17}. We did not analyze the domains of FSFI individually but overall sexual dysfunction was found in 50.1% of the patients comparable to 49.3% in study of Alia et al.

Costa et al in 2015 determined the sexual function rather dysfunction among women with RA. The differentiating theme of their study was that they only included new onset cases i.e. those with <1 year of diagnosis of rheumatoid arthritis. More than 75% of their patients suffered from sexual dysfunction which was really alarming as usually sexual health is not the area of focus for the treating physician and focus is mainly laid on the pain symptoms\textsuperscript{18}. More than half of our patients had sexual dysfunction when screened on FSFI but still our results were quite less than Costa et al.

Khnaba et al in 2016 in a similar study concluded sexual problems were common among the patients suffering from RA as compared to the controls. Presence of clinical depression and inadequately managed pain were the factors related to presence of sexual dysfunction among their study participants\textsuperscript{19}. Ours was not a case control study so comparison was not made but still high frequency of sexual dysfunction among the women suffering from RA support the results generated by Khnaba et al.

**LIMITATION OF STUDY**

One major limitation of our study has been the use of self-reported screening tool for assessing the
sexual dysfunction. Under reporting or over reporting of symptoms may occur on the self-reporting tools. Some comorbid conditions were part of exclusion criteria and some were studied as an independent variable in the final analysis. History taking was the only source to ascertain these conditions. Medical records or fresh investigations were not carried out to confirm the comorbid conditions among the study participants. Future studies may address these limitations and generate results which could be generalized to the local population.

CONCLUSION

High reporting of sexual dysfunction among the women suffering from rheumatoid arthritis indicates that this has been a neglected phenomenon by the physicians and researchers and may be added in routine screening. Women with long duration of illness and those managed with more than one drugs should be focused more while screening for sexual problems.

CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any author.

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