Chronic Pain Assessment in Moroccan Hemodialysis Population

Ibtihale Boukhira 1*, Said Jidane 1, Ahmed Kharbach 2, Lahcen Belyamani 1

1 Research team in analgesia and local loco anesthesia, Faculty of Medicine and Pharmacy of Rabat, University Mohamed 5, Rabat, MOROCCO
2 Laboratory of Biostatistics, Clinical Research and Epidemiology (LBRCE), Faculty of Medicine and Pharmacy of Rabat, Mohammed V University of Rabat, MOROCCO
*Corresponding Author: ibtihalee@gmail.com

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ABSTRACT
Introduction: This study aims to assess the prevalence, as well as the impact of chronic pain on the daily life of hemodialysis patients and to determine the associated socio-demographic, clinical-biological, and psychological factors.

Methods: This study was a cross-sectional study that included 441 hemodialysis patients. The characteristics of the chronic pain were collected by the Brief Pain Inventory questionnaire and by the visual analog scale. The anxious and depressed mood was assessed by the Hospital Anxiety and Depression Scale, factors associated with chronic pain were determined through univariate and multivariate analysis.

Results: the prevalence of chronic pain was 72.8%. It was severe in 40.8% of cases and it completely interfered with general activity in 72.9% of cases. The most frequently reported pain site was: lowers extremities (39.9%). Thus, 59.9% of patients reported using analgesics, with a frequent intake in 74.3% of cases. Anxiety and depression were found respectively in 68% and 66% of cases. The chronic pain was significantly associated with depression (p<0.001), anxiety (p<0.001), living conditions (p<0.001), level of studies (p<0.001), and marital status (p=0.020).

Conclusion: A multidisciplinary approach is recommended for the management of chronic pain, involves Nurses, physiotherapists, psychologists, health educators and family.

Keywords: chronic pain, hemodialysis, assessment, associated factors

INTRODUCTION
Chronic pain is a common, complex, and distressing problem that has a profound impact on individuals and society [1]. Indeed, it's a source of disability, major social and psychological alterations [2], and even more in hemodialysis patients.

The prevalence of chronic pain in hemodialysis patients was up to 82% and 92% [3,4], and it is severe to moderate in about 35% to 70% of these patients [4].

However, in chronically hemodialyzed population, most patients are not evaluated for these aspects and therefore not sufficiently treated [5]. Health professionals should therefore understand and relieve pain in this population, in order to improve their quality of life and care [4]. Chronic pain must be understood in the context of social, biological, psychological, and physical factors in order to develop treatment plans and prevention strategies [1]. It is important to analyze these different factors for adequate and holistic pain management.

This study aims to assess the prevalence, as well as the impact of chronic pain on the daily life of hemodialysis patients, in order to determine the associated socio-demographic, clinical-biological, and psychological factors.

PATIENTS AND METHODS

Ethics Approval and Consent to Participate
The study has been approved by the ethics committee for biomedical research of the MOHAMMED V Faculty of Medicine and Pharmacy in RABAT (N/R: Folder Number 10/20), and informed consent was obtained from each subject.

Design and Study Area
This is a multicenter cross-sectional study conducted from February 2020 to September 2020 including all hemodialysis patients (n=441) recruited from all public sectors hemodialysis centers (6 centers) in Souss Massa region, Morocco.

Inclusion and Exclusion Criteria
Patients satisfying the following criteria were included in this study consecutively: age greater than 18 years old, Moroccan nationality, time on hemodialysis greater than three months, absence of a recent change in the usual lifestyle, and a prior agreement. They will be excluded in this study: Hemodialysis patients who are comatose, delusional and non-consenting.

Chronic Pain Definition
Pain is defined by duration, it is considered chronic if it persists more than three months [6], From this criterion and based on the pain syndrome, we divided our population into
two groups, according to the presence or absence of chronic pain.

**Instrument and Data Collection**

Basic demographic data were collected, including information about age, gender, health cover, level of education, marital status, professional one, and living conditions. Baseline clinical, hematological, dialytic, and psychological data of these patients were also collected: clinical (causal nephropathy, associated comorbidities, body mass index, toxic habits, and respect of hygierno-dietetic rules), biological (hemoglobin, phosphatemia, albumin, C-reactive protein, mean calcium level, thyroid assessment), dialytic (duration of hemodialysis, number of dialysis sessions, Interdialytic Weight Gain, Vascular Access, and Renal therapy replacement), and psychological (depression and anxiety).

In this study, the characteristics of the chronic pain were collected by the BPI questionnaire: Brief Pain Inventory (Short Form), with the Arabic version which is already validated [7], (type, intensity, site, frequency, origin, psycho-affective impact on the daily life of hemodialysis patients).

Pain intensity was assessed using the visual analog scale (VAS) allowing patients to choose a number from 0 to 10 to describe the degree of their chronic pain, then it was classified as absent for a score of 0, low for a score from 1 to 3, moderate for a score of 4 to 6, severe for a score of 7 to 9 and unbearable for a score of 10. Regarding the frequency, chronic pain is considered as permanent if it was present continuously without no-pain interval, daily if it occurs at least once a day, intermittent if it occurs less than once a day, and finally, rare when it occurs less than once a week.

The HADS scale (Hospital Anxiety and Depressive scale) in its already validated Arabic version [8] is used to detect depression and anxiety in our population. It is a reliable instrument to verify the presence or absence of depression and anxiety and can even measure the severity of anxiety and depressive disorders [9]. It comprises 14 items graded from 0 to 3. Seven questions relate to anxiety (total A) and seven others to the depressive dimension (total D), thus, making it possible to obtain two scores (maximum score for each score = 21). The anxiety score is obtained by adding the scores assigned to the questions on anxiety. A score greater than or equal to 11 defines anxiety. The depression score is obtained by adding the scores assigned to the seven questions on depression. A score greater than or equal to 11 defines depression [9].

**Data Management and Statistical Analysis**

The qualitative variables were presented as frequency and percentages, and mean ± standard deviation (SD) or median (interquartile range, IQR) for quantitative variables. The Chi-square test ($\chi^2$) or Fisher’s exact test, were performed according to their particular application conditions, to examine for differences in proportions of categorical variables between two groups (the group with chronic pain and the group that does not complain of any chronic pain). Furthermore, univariate and multivariate logistic regression analyses were done to identify the factors associated with chronic pain. All independent variables with a P-value < .25 in the univariate analysis were taken into account in the multivariate logistic regression analysis.

The difference is considered statistically significant for a P < .05. Data management and statistical analysis was done using the SPSS for Windows software package (ver. 13.0; SPSS Inc., Chicago, IL, USA).

**RESULTS**

**Characteristics of the Study Population**

The total included in the study was 441 of chronic hemodialysis patients, with a mean age of 56.05 (15.67). Elderly subjects (≥ 65 years) represented 30.6 % of patients (n = 135). The sex ratio M / F was 1.29 (249 M / 192 F), the majority (63.7 %) of the participants was illiterate. 61.2 % of patients were living alone or with one person in their house and almost all of the participants (85 %) were unemployed. There were 300 (68 %) patients who self-reported anxiety, and 291 (66 %) depression. However, only 2.7 % reported using anxiolytics and 2.3 % antidepressants. Table 1 summarizes all the socio-demographic and psychological characteristics of patients.

The mean body mass index (BMI) was 23.18 (3.6) and the median is 24.03 (21.60– 25.90) kg / m². The mean and median duration of hemodialysis are 64.84 ± 49.67 months and 56 (IQR 28–84) months, respectively. The etiologies of end-stage

| Variable | All patients N (%) | Chronic pain N (%) | No Chronic pain N (%) | P value |
|----------|--------------------|--------------------|-----------------------|---------|
| Age      |                    |                    |                       |         |
| [18-45 years] | 56.05 ± 15.67 | 57.04 ±15.28 | 52.40 ± 16.16 | <0.01*  |
| [46-65 years] | 193 (43.8) | 144 (32.7) | 49 (11.1) |         |
| >65 years | 135 (30.6) | 107 (24.3) | 28 (6.3) |         |
| Gender   |                    |                    |                       | 0.072   |
| Male     | 249 (56.5) | 174 (39.5) | 75 (17) |         |
| Female   | 192 (43.5) | 147 (33.3) | 45 (10.2) |         |
| Level of studies |                |                    |                       | <0.01*  |
| Illiterate | 281 (63.7) | 206 (46.2) | 75 (16.2) |         |
| Primary  | 79 (17.9) | 35 (7.9) | 37 (7.6) |         |
| Middle school | 36 (8.2) | 16 (3.7) | 20 (4.4) |         |
| Hight school | 41 (9.3) | 30 (6.8) | 11 (2.5) |         |
| Higher education | 4 (0.9) | 2 (0.4) | 2 (0.4) |         |
| Professional status |           |                    |                       | 0.321   |
| Employee | 51 (11.6) | 33 (10.3) | 18 (5) |         |
| Self employed | 12 (2.7) | 7 (2.2) | 5 (1.2) |         |
| Inactive | 375 (85) | 279 (63.9) | 96 (21.8) |         |
| Retireme  | 3 (0.7) | 2 (0.4) | 1 (0.2) |         |

* The Chi-square test ($\chi^2$) or Fisher’s exact test; HADS: Hospital Anxiety and Depressive scale.

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Table 1. Socio-demographic and psychological characteristics of the patients classified according to the presence of chronic pain.
Table 1 (continued). Socio-demographic and psychological characteristics of the patients classified according to the presence of chronic pain

| Variable                        | All patients | Chronic pain | No Chronic pain | P value |
|---------------------------------|--------------|--------------|-----------------|---------|
| Marital status                  |              |              |                 |         |
| Single                          | 61 (13.8)    | 33 (7.5)     | 28 (23.3)       | <0.01*  |
| Married                         | 297 (67.3)   | 218 (67.9)   | 79 (65.8)       |         |
| Divorced                        | 7 (1.6)      | 5 (1.6)      | 2 (1.7)         |         |
| Widower                         | 76 (17.2)    | 65 (20.2)    | 11 (9.2)        |         |
| Living conditions               |              |              |                 |         |
| living alone                    | 270 (61.2)   | 161 (50.2)   | 11 (9.2)        | <0.01*  |
| living with others              | 171 (38.8)   | 160 (49.8)   | 109 (90.8)      |         |
| Health coverage                 |              |              |                 |         |
| With assurance                  | 431 (97.9)   | 311 (96.88)  | 120 (100)       | 0.040*  |
| Without assurance               | 10 (2.3)     | 10 (0.03)    | 0               |         |
| Anxiety                         |              |              |                 |         |
| Yes (Score HADS ≥11)            | 300 (68)     | 267 (83.2)   | 33 (16.8)       | <0.01*  |
| No (Score HADS <11)             | 41 (32)      | 54 (16.8)    | 87 (72.5)       |         |
| Depression                      |              |              |                 |         |
| Yes (Score HADS ≥11)            | 291 (65)     | 258 (80.4)   | 33 (27.5)       | <0.01*  |
| No (Score HADS <11)             | 150 (34)     | 63 (19.6)    | 87 (79.2)       |         |
| Use of anxiety medications      | 12 (2.7)     | 10 (3.1)     | 2 (1.7)         | 0.322   |
| Use of depression medications   | 10 (2.3)     | 8 (2.5)      | 2 (1.7)         | 0.280   |

* The Chi-square test (x2) or Fisher’s exact test; HADS: Hospital Anxiety and Depressive scale

Table 2. Clinical and dialytic characteristics of the patients classified according to the presence of chronic pain

| Variable                        | All patients | Chronic pain | No chronic pain | P value |
|---------------------------------|--------------|--------------|-----------------|---------|
| Respect of hygieno-dietetic rules | 10 (2.3)     | 8 (2.5)     | 2 (1.7)         | 0.459   |
| Toxic Habits                    | 17 (3.9)     | 17 (5.3)    | 0 (0)           | 0.040   |
| Body Mass Index (Kg/m2)         |              |              |                 | 0.798   |
| <18.5                           | 74 (16.8)    | 52 (16.2)   | 22 (18.3)       |         |
| 18.5-24.9                       | 241 (54.6)   | 175 (54.5)  | 66 (55)         |         |
| 25-29.9                         | 126 (28.8)   | 94 (29.3)   | 32 (26.7)       |         |
| Co-morbidity                    |              |              |                 |         |
| Hypertension                    | 235 (53.3)   | 177 (55.1)  | 58 (48.3)       | 0.121   |
| Diabetes mellitus               | 165 (37.4)   | 129 (40.2)  | 36 (30)         | 0.031   |
| Cardiovascular diseases         | 19 (4.3)     | 16 (5)      | 3 (2.5)         | 0.192   |
| System diseases                 | 4 (0.9)      | 3 (0.9)     | 1 (0.8)         | 0.279   |
| Cancer                          | 4 (0.9)      | 3 (0.7)     | 1 (0.2)         | 0.701   |
| Liver diseases                  | 3 (0.7)      | 2 (0.6)     | 1 (0.8)         | 0.615   |
| A prior stroke history          | 32 (7.3)     | 26 (8.1)    | 6 (1.4)         | 0.183   |
| Causal Nephropathy              |              |              |                 |         |
| Indeterminate nephropathy       | 147 (33.3)   | 92 (28.7)   | 55 (45.8)       | <0.01*  |
| Diabetic nephropathy            | 180 (40.8)   | 143 (44.5)  | 37 (30.8)       | 0.006*  |
| Glomerular chronic              | 42 (9.5)     | 32 (10)     | 10 (8.3)        | 0.375   |
| Vascular Nephropathy            | 29 (6.6)     | 25 (7.8)    | 4 (3.3)         | 0.066   |
| Polycystic kidney disease       | 13 (2.9)     | 10 (3.1)    | 3 (2.5)         | 0.509   |
| Tubulo-interstitial nephritis   | 20 (4.5)     | 13 (4)      | 7 (5.8)         | 0.285   |
| Eclampsia                       | 4 (0.9)      | 2 (0.6)     | 2 (1.7)         | 0.299   |
| Renal therapy replacement       |              |              |                 |         |
| Hemodialysis                    | 441 (100)    | 321 (100)   | 120 (100)       | 0.273   |
| Interdialytic Weight Gain /Kg   |              |              |                 |         |
| < 1                             | 2.38±1.05    | 2.46±1.06   | 2.17±0.98       | 0.233   |
| 1—2                            | 205 (46.5)   | 146 (45.5)  | 59 (49.2)       |         |
| >2                             | 155 (35.1)   | 120 (37.4)  | 35 (29.2)       |         |
| Duration on hemodialysis /mouths|              |              |                 | 0.152   |
| <50                            | 64.8±49.67   | 65.6±49.59  | 62.7±50.02      |         |
| 50 -100                        | 208 (47.2)   | 147 (45.8)  | 61 (50.8)       |         |
| >100                           | 152 (34.5)   | 119 (37.1)  | 33 (27.5)       |         |
| Number of dialysis sessions / week | 81 (18.4) | 55 (17.1) | 26 (21.7) |         |
| 2 Sessions                     | 399 (90.5)   | 302 (94.1)  | 97 (80.8)       | <0.01*  |
| 3 Sessions                     | 42 (9.5)     | 19 (5.9)    | 23 (19.2)       |         |
| Vascular Access                 |              |              |                 |         |
| AVF proximal                    | 131 (29.7)   | 100 (31.2)  | 31 (25.8)       | 0.273   |
| AVF distal                      | 293 (66.4)   | 211 (65.7)  | 82 (68.3)       |         |
| Tunnelled jugular catheter      | 17 (3.9)     | 10 (3.1)    | 7 (5.8)         |         |

* The Chi-square test (x2) or Fisher’s exact test

Chronic renal failure (ESRD) and the list of recorded comorbidities are summarized in Table 2. Approximately 90.5% of patients (n = 399/441) had a frequency of 2 sessions of 4 to 4.5 hours dialysis per week, while the remaining 42 (9.5%) were
Prevalence of Chronic Pain

Of the 441 patients, 321 reported the presence of chronic pain (CP), for a prevalence of 72.8 %. In the group with chronic pain (CP +): The mean age is 57.04 (15.28), the sex ratio is 174H / 147F, 206 patients (64.2 %) were illiterate, 279 (86.9 %) were unemployed, the mean duration of dialysis was 65.64(49.59) months (see Table 1). There were 267 (80.4 %) who self-reported anxiety and 211 (65.7 %) depression. There were 267 (80.4 %) who self-reported anxiety and 211 (65.7 %) depression. The chronic pain described by the patients was in the head in 14 %, in the abdomen in 11.2 %, multifocal in 10 %, in the lower extremities in 39.9 % of the cases, in the back in 19.3 %, in the shoulders in 5.6 %, and with an average number of painful sites per patient of 4.41 (1.24). Thus, the identified causes of chronic CP are the following: osteoarticular, neurological, vascular, digestive and post-traumatic in respectively 155 (48.3 %), 83 (25.9 %), 45 (14 %), 35 (10.9 %), 3 (0.9 %) (See Table 4).

Characteristics of Chronic Pain

Chronic pain intensity was absent, mild, moderate, severe and unbearable in 1 (0.3 %), 69 (21.5 %), 110 (34.3 %), 131 (40.8 %), and 10 (3.1 %) of patients respectively. Its frequency was mostly intermittent (61.7 %). However, pain was only worsened during dialysis sessions in 9.6 % of cases.

The chronic pain described by the patients was in the lowers extremities in 39.9 % of the cases, in the back in 19.3 %, in the head in 14 %, in the abdomen in 11.2 %, multifocal in 10 %, in the shoulders in 5.6 %, and with an average number of painful sites per patient of 4.41 (1.24). Thus, the identified causes of chronic CP are the following: osteoarticular, neurological, vascular, digestive and post-traumatic in respectively 155 (48.3 %), 83 (25.9 %), 45 (14 %), 35 (10.9 %), 3 (0.9 %) (See Table 4).

Analgesic Admission

We will retain 191 patients, approximately (59.9 %), had taking analgesics and up to 59.9 % of patients taking analgesics frequently in 74.3 % of cases, daily in 23.6 % of cases and rarely in 2.4 % of cases. 92.1 % of analgesics are level 1 and 7.9 % are level 2 and no level 3 analgesic is used. This admission only allowed complete relief in 6 % of cases and the degree of relief remains low in 131 patients (68.6 %). The consequent analgesic admission is summarized in Table 4.

### Table 3. Biological characteristics of the patients classified according to the presence of chronic pain

| Variable                  | All patients N (%) | Chronic pain N (%) | No chronic pain N (%) | P value |
|---------------------------|--------------------|--------------------|-----------------------|---------|
| Hemoglobin (g/dl)         | 9.65±1.58          | 9.72±1.54          | 9.46±1.67             | 0.196   |
| <8                       | 51 (11.6)          | 34 (10.6)          | 17 (14.2)             |         |
| 8-10,9                   | 289 (65.5)         | 207 (64.5)         | 171 (66.8)            |         |
| ≥11                      | 101 (22.9)         | 80 (24.9)          | 21 (17.5)             |         |
| PTH (mg/ml)              | 476.17±216.97      | 482.90±216.94      | 458.17±216.91         | 0.884   |
| < 300                    | 136 (30.8)         | 99 (30.8)          | 37 (30.8)             |         |
| 300—600                  | 214 (48.5)         | 154 (48)           | 60 (50)               |         |
| > 600                    | 91 (20.6)          | 68 (21.2)          | 23 (19.2)             |         |
| Ca(mmol/l)               | 51.05±31.46        | 49.53±30.08        | 55.12±32.74           | 0.022*  |
| <90                      | 393 (89.1)         | 294 (91.6)         | 99 (82.5)             |         |
| >90                      | 40 (9.1)           | 22 (6.9)           | 18 (15)               |         |
| >105                     | 8 (1.8)            | 5 (1.6)            | 3 (2.5)               |         |
| PO4(mg/l)                | 46.83±16.48        | 46.39±15.78        | 46.43±18.28           | 0.133   |
| <25                      | 17 (3.9)           | 9 (2.8)            | 8 (6.7)               |         |
| 25-45                    | 247 (56)           | 185 (57.6)         | 62 (51.7)             |         |
| >45                      | 177 (40.1)         | 127 (39.6)         | 50 (41.7)             |         |
| Albumin (g/l)            | 42.75±14.68        | 42.78±14.52        | 42.66±15.18           | 0.884   |
| <38                      | 136 (30.8)         | 99 (30.8)          | 37 (30.8)             |         |
| 38-50                    | 214 (48.5)         | 154 (48)           | 60 (50)               |         |
| >50                      | 91 (20.6)          | 68 (21.2)          | 23 (19.2)             |         |
| CRP (mg/l)               | 63.27±28.34        | 64.85±28.38        | 59.05±27.91           | 0.321   |
| <6                       | 51 (11.6)          | 33 (10.3)          | 18 (15)               |         |
| 6-50                     | 12 (2.7)           | 7 (2.2)            | 5 (4.2)               |         |
| 50-100                   | 375 (85)           | 279 (86.9)         | 96 (80)               |         |
| >100                     | 3 (0.7)            | 2 (0.6)            | 1 (0.8)               |         |

* The Chi-square test (x2) or Fisher’s exact test

### Table 4. Characteristics of chronic pain and Analgesic admission

| Variable                  | Frequency N (%) |
|---------------------------|-----------------|
| Intensity of chronic pain |                 |
| Absent: VAS at 0          | 1 (0.3)         |
| Mild: VAS from 1 to 3     | 69 (21.5)       |
| Moderate: VAS from 4 to 6 | 110 (34.3)      |
| Severe: VAS from 7 to 9   | 131 (40.8)      |
| Unbearable: VAS at 10     | 10 (3.1)        |
| Pain frequency            |                 |
| Intermittent              | 198 (61.7)      |
| Daily                     | 73 (22.7)       |
| Permanent                 | 46 (14.3)       |
| Rare                      | 4 (1.2)         |
| Causes of chronic pain    |                 |
| Osteo-arthicular          | 155 (48.3)      |
| Neurologic                | 83 (25.9)       |
| Vascular                  | 45 (14)         |
| Digestive                 | 35 (10.9)       |
| Post-traumatic            | 3 (0.9)         |
| Painful region            |                 |
| Head                      | 45 (14)         |
| Shoulders                 | 18 (5.6)        |
| Abdomen                   | 36 (11.2)       |
| Back                      | 62 (19.3)       |
| Lower limb                | 128 (39.9)      |
| Multifocal pain           | 32 (10)         |

VAS: visual analog scale
Impact of Chronic Pain

The impact of chronic pain on the daily life of patients is summarized in Table 5. Note that it completely interfered with general activity, with the ability to walk and usual work in 234 patients (72.9%), 221 (68.85%), 230 (71.7%) respectively. Regarding the mood, the relations with others and the enjoyment of life, chronic pain is completely embarrassing 69.8% (224 patients), 34% (109 patients) and 34.6% (111 patients) of cases respectively.

Factors Associated with Chronic Pain

Univariate analysis

1. Socio-demographic and psychological factors on univariate analysis (See Table 6)

2. Clinical factors on univariate analysis (See Table 7)

3. Biological and dialytic factors on univariate analysis (See Table 8)

Table 5. Impact of chronic pain

| Variable                     | No gene N (%) | Weak gene N (%) | Moderate gene N (%) | Important gene N (%) | Complete gene N (%) |
|------------------------------|---------------|-----------------|---------------------|----------------------|---------------------|
| General activity             |               |                 |                     |                      |                     |
| Ability to walk              |               |                 |                     |                      |                     |
| Usual Work                   |               |                 |                     |                      |                     |
| Sleep                        |               |                 |                     |                      |                     |
| Mood                         |               |                 |                     |                      |                     |
| Relations with others people |               |                 |                     |                      |                     |
| Enjoyment of life            |               |                 |                     |                      |                     |

Table 6. Socio-demographic and psychological factors associated with chronic pain on univariate analysis

| Variable                  | OR   | CI 95%           | P value |
|---------------------------|------|------------------|---------|
| Age [18-45 years]         | 2.34 | 1.33-4.12        | <0.01   |
| [46-65 years]             | 1.30 | 0.76-2.20        | 0.329   |
| >65 years                 | 1    |                  |         |
| Sexe Male                 | 1.40 | 0.91-2.16        | 0.119   |
| Female                    | 1    |                  |         |
| Level of studies          |      |                  |         |
| Illiterate                | 0.12 | 0.01-1.18        | 0.070   |
| Primary                   | 0.09 | 0.01-1.00        | 0.050   |
| Middle school             | 0.29 | 0.02-3.14        | 0.314   |
| Hight school              | 0.06 | 0.00-0.76        | 0.029   |
| Professional status       |      |                  |         |
| Employee                  | 1.09 | 0.09-12.87       | 0.945   |
| Self employed             | 1.71 | 0.10-20.43       | 0.793   |
| Inactive (unemployed)     | 0.68 | 0.06-7.67        | 0.761   |
| Retirement                | 1    |                  |         |
| Marital status            |      |                  |         |
| Single                    | 5.01 | 2.22-11.31       | <0.01   |
| Married                   | 2.14 | 1.07-4.26        | 0.030   |
| Divorced                  | 2.36 | 0.40-13.73       | 0.338   |
| Widower                   | 1    |                  |         |
| Living conditions         |      |                  |         |
| Living alone              | 9.84 | 5.10-19.00       | <0.01   |
| Living with others        | 1    |                  |         |
| Health coverage           |      |                  |         |
| With assurance            | 0.17 | 0.03-0.83        | 0.99    |
| Without assurance         | 1    |                  |         |
| Anxiety                   |      |                  |         |
| Yes (Score HADS ≥11)      | 13.03| 7.93-21.40       | <0.01   |
| No (Score HADS <11)       | 1    |                  |         |
| Depression                |      |                  |         |
| Yes (Score HADS ≥11)      | 10.79| 6.63-17.55       | <0.01   |
| No (Score HADS <11)       | 1    |                  |         |

OR: Odds Ratio; CI: Confidence interval, HADS: Hospital Anxiety and Depressive scale
Table 7. Clinical factors associated with chronic pain on univariate analysis

| Variable                                      | OR     | CI 95%        | P value |
|-----------------------------------------------|--------|---------------|---------|
| Respect hygieno-dietetic rules                |        |               |         |
| Yes                                           | 0.89   | 0.09-8.64     | 0.921   |
| No                                            | 1      |               |         |
| Toxic Habits                                   |        |               |         |
| Yes                                           | 0.16   | 0.03-0.17     | 0.998   |
| No                                            | 1      |               |         |
| Body Mass Index (kg/m²)                        |        |               |         |
| <18.5                                         | 0.48   | 0.65-2.35     | 0.506   |
| 18.5-24.9                                     | 0.32   | 0.67-1.81     | 0.683   |
| 25-29.9                                       | 1      |               |         |
| Hypertension                                  |        |               |         |
| Yes                                           | 1.31   | 0.86-2.00     | 0.203   |
| No                                            | 1      |               |         |
| Diabetes mellitus                             |        |               |         |
| Yes                                           | 0.63   | 0.40-1.00     | 0.050   |
| No                                            | 1      |               |         |
| Cardiovascular diseases                       |        |               |         |
| Yes                                           | 0.48   | 0.14-1.70     | 0.262   |
| No                                            | 1      |               |         |
| Systemic diseases                             |        |               |         |
| Yes                                           | 0.000  | 0.00-0.71     | 0.999   |
| No                                            | 1      |               |         |
| Cancer                                        |        |               |         |
| Yes                                           | 0.89   | 0.09-8.64     | 0.921   |
| No                                            | 1      |               |         |
| Liver diseases                                |        |               |         |
| Yes                                           | 1.34   | 0.12-23.13    | 0.812   |
| No                                            | 1      |               |         |
| A prior stroke history                        |        |               |         |
| Yes                                           | 0.59   | 0.24-1.48     | 0.269   |
| No                                            | 1      |               |         |
| indeterminate nephropathy                     |        |               |         |
| Yes                                           | 2.10   | 1.36-3.24     | <0.01   |
| No                                            | 1      |               |         |
| Diabetic nephropathy                          |        |               |         |
| Yes                                           | 0.55   | 0.35-0.86     | 0.010   |
| No                                            | 1      |               |         |
| Glomerular chronic nephropathy                |        |               |         |
| Yes                                           | 0.82   | 0.39-1.72     | 0.603   |
| No                                            | 1      |               |         |
| Vascular Nephropathy                          |        |               |         |
| Yes                                           | 0.40   | 0.13-1.19     | 0.103   |
| No                                            | 1      |               |         |
| Polycystic kidney disease                     |        |               |         |
| Yes                                           | 0.79   | 0.21-2.94     | 0.734   |
| No                                            | 1      |               |         |
| Tubulo-interstitial nephritis                 |        |               |         |
| Yes                                           | 0.57   | 0.57-3.77     | 0.426   |
| No                                            | 1      |               |         |
| Eclampsia                                     |        |               |         |
| Yes                                           | 2.70   | 0.37-19.41    | 0.323   |
| No                                            | 1      |               |         |

Table 8. Biological and dialytic factors associated with chronic pain on univariate analysis

| Variable                                      | OR     | CI 95%        | P value |
|-----------------------------------------------|--------|---------------|---------|
| Dialytic parameters                           |        |               |         |
| Interdialytic Weight Gain (IDWG)              |        |               |         |
| < 1kg                                         | 0.85   | 0.49-1.49     | 0.580   |
| 1—2 Kg                                       | 0.61   | 0.33-1.12     | 0.114   |
| >2Kg                                         | 1      |               |         |
| Duration on hemodialysis /mouths              |        |               |         |
| <50                                          | 0.67   | 0.50-1.52     | 0.645   |
| 50-100                                       | 0.58   | 0.32-1.07     | 0.084   |
| >10                                          | 1      |               |         |
| Number of dialysis sessions / week            |        |               |         |
| 2 Sessions                                   | 0.26   | 0.13-0.50     | <0.01   |
| 3 Sessions                                   | 1      |               |         |

OR: odds ratio, CI: confidence interval
Multivariate analysis

The variables that were included in the regression equation were: age, sexe, education level, marital status, living conditions, duration of hemodialysis, inter-dialytic weight gain, Number of dialysis sessions per week, comorbidities (hypertension, diabetes and cardiovascular diseases), Haemoglobin, Calcemia, indeterminate nephropathy, Diabetic nephropathy, Vascular Nephropathy, vascular access, anxiety and depression.

The results of the multivariate analysis revealed, among all the variables, five factors which had a strong statistical correlation ($P < .05$) with chronic pain in hemodialysis patients: depression, anxiety, education level, marital status and living conditions (See Table 9).

Table 8 (continued). Biological and dialytic factors associated with chronic pain on univariate analysis

| Variable                          | OR     | CI 95%        | $P$ value |
|-----------------------------------|--------|---------------|-----------|
| Vascular Access                   |        |               |           |
| AVF proximal                      | 0.44   | 0.15-1.26     | 0.127     |
| AVF distal                        | 0.55   | 0.20-1.50     | 0.248     |
| Tunneled jugular catheter         | 1      |               |           |
| Hematology parameters             |        |               |           |
| Hemoglobin (g/dl)                 |        |               |           |
| <8                                | 1.90   | 0.89-4.05     | 0.094     |
| 8-10.9                            | 1.50   | 0.87-2.60     | 0.138     |
| $\geq11$                          | 1      |               |           |
| PTH (pg/ml)                       |        |               |           |
| <300                              | 1.10   | 0.60-2.02     | 0.746     |
| 300-600                           | 1.15   | 0.65-2.01     | 0.320     |
| $>600$                            | 1      |               |           |
| Ca(mmol/l)                        |        |               |           |
| <90                               | 0.56   | 0.13-2.39     | 0.435     |
| 90-105                            | 1.36   | 2.28-6.49     | 0.697     |
| $>105$                            | 1      |               |           |
| PO4(mg/l)                         |        |               |           |
| <25                               | 2.25   | 0.82-6.18     | 0.113     |
| 25-45                             | 0.85   | 0.55-1.31     | 0.469     |
| $>45$                             | 1      |               |           |
| Albumin (g/l)                     |        |               |           |
| <38                               | 1.10   | 0.60-2.02     | 0.746     |
| 38-50                             | 1.15   | 0.65-2.01     | 0.620     |
| $>50$                             | 1      |               |           |
| CRP (mg/l)                        |        |               |           |
| <6                                | 1.09   | 0.09-12.87    | 0.945     |
| 6-50                              | 1.42   | 0.10-20.43    | 0.793     |
| 50-100                            | 0.68   | 0.06-7.67     | 0.761     |
| $>100$                            | 1      |               |           |

OR: odds ratio, CI: confidence interval

Table 9. Factors associated with chronic pain on multivariate analysis

| Variable | aOR     | CI 95%        | $P$ value |
|----------|---------|---------------|-----------|
| Level of studies |        |               |           |
| High school     | 0.01   | 0.00-0.28     | <0.001    |
| Marital status  |        |               |           |
| Single           | 0.37   | 1.40-49.83    | 0.020     |
| Living conditions|        |               |           |
| Single           | 24.04  | 8.46-68.32    | <0.001    |
| Anxiety          |        |               |           |
| Yes              | 19.91  | 8.17-48.50    | <0.001    |
| Depression       |        |               |           |
| Yes              | 20.74  | 9.13-17.10    | <0.001    |

aOR: Adjusted odds ratio, CI: confidence interval

DISCUSSION

Prevalence of Chronic Pain

The prevalence of chronic pain in this study is 72.8 %, it is almost similar to 70.9 % in the study of Elharraqui [10], 74.4 % in Sadigova’s work [5], 82 % in the Flesherman series [3], while in other series [11-13], this rate does not exceed 50.1 %. This difference may be justified by the difference between the contexts of the assessment and management approaches of chronic pain, but also by the differences in the perception of pain in different countries, different cultures and different ethnicities. Several studies have reported that there are large and complex cultural variations between countries and ethnicities in the prevalence and outcomes of pain-related conditions [14,15], another study showed that the prevalence of chronic pain and its disability is more important in underdeveloped countries than in developed ones [16].
Chronic Pain Assessment

In this study, the identified causes of chronic pain are as follows: osteoarticular, neurological, vascular, digestive and post-traumatic in respectively 155 (48.3 %), 83 (25.9 %), 45 (14 %), 35 (10.9 %), 3 (0.9 %). In fact, 82% of chronic kidney disease patients undergoing dialysis have been reported to have chronic pain [11] due to the frequent osteoarticular, cardiovascular, digestive, and traumatic complications in this population [17]. The main cause of chronic pain in our patients is osteoarticular (48.3 %), as reported in some trials [13,18].

The pain associated with osteoarticular complications in chronic dialysis patients can be explained by β2-microglobulin amyloidosis. The presence of amyloid deposits fibrillary mainly in joint tissues and in bones, clinically causes the appearance of osteoarticular pain syndromes [19]. Therefore, early and optimal management of disorders bone mineral linked to Chronic Renal Insufficiency was expected to reduce in part of the occurrence of these difficulties [13]. In our cases, the intensity of the pain was significant with 40.8 % of severe form versus 44 % in the Bouaatar study [12], and 53.3 % in the Ben-Bassat study [20]. Multiple studies indicated a high prevalence of patients with moderate or severe pain [4]. The most common painful site was in the lower limbs in 39.9 % of patients, as reported in other studies [5,13,20], the pain was only worsened during dialysis sessions in 9.6 % of cases.

Analgesic Admission

Although more than half (59.5 %) of patients had regular use of level 1 and level 2 analgesics, complete relief was only noted in 3.1 % of patients. Results of several studies show insufficient relief of Chronic Pain in hemodialysis patients with analgesics [5]. This finding may be justified by the lack of knowledge of the exact mechanism of Chronic Pain for an adequate prescription of analgesics or opioids in chronic hemodialysis patients [21]. However, special considerations should be taken in hemodialysis patients to minimize direct renal complications induced by analgesics and other complications related to drug accumulation due to reduced renal clearance [22].

In addition, studies prove that drug treatment remains insufficient in face of chronic pain in hemodialysis patients. [23,24]. In this regard, other non-pharmacological treatments could improve the pain, depression, anxiety, functionality and quality of life of hemodialysis patients with chronic pain without a major adverse event [24]. It has been proven that there are non-drug analgesic approaches that can alleviate chronic pain in hemodialysis patients such as conscious calming gestures [23], cognitive behavioral therapies [2], and hypnosis: several local experiences have highlighted the benefits of hypnosis for controlling acute and chronic pain in hemodialysis patients [25].

Impact of Chronic Pain on Daily Life

In this study, Chronic pain caused complete discomfort in general activity in 72.9 % of cases versus 62.1 % in the study by El Harraqui [10], on the ability to walk in 68.85 % of cases. This rate varies from 19.1 % to 44.1 % in other studies [12, 13]. Also, usual work is completely hampered by chronic pain in 71.7 % of cases. Indeed, several authors have reported that chronic pain disrupts body patterns, reduces overall activity level, and causes intolerance to physical and/or intellectual effort [2,26], chronic pain is, therefore, a source of disability, and major alterations in daily life [2]. Furthermore, due to chronic pain complete sleep discomfort was noted in 38.01 % of cases, several studies prove that chronic pain is significantly associated with sleep disorders and even insomnia in hemodialysis patients [11,18,27,28]. Chronic pain is a multidimensional phenomenon that has several components: physical, psychological, and social. If left untreated, it can affect several aspects: mood, enjoyment of life, and relationship with others [11]. In our study, these aspects are completely affected in 69.80 %, 34.6 % and 34 % respectively. Chronic pain can therefore only be evaluated in a relevant way if it is listened to, observed, but also analyzed through the repercussions that are personal, physical, and psychological, as well as social and professional [26].

Factors Associated with Chronic Pain

Multivariate analysis in our study showed a strong correlation between chronic pain and five factors: depression, anxiety, education level, marital status and living conditions. For the first two factors, several authors have reported that the comorbidity of depression and anxiety are common in chronically painful people, and people with chronic pain are more likely to have depressive and anxious symptoms than people without pain [29,30].

Several investigators have estimated that depression occurs in about 20 % to 67 % of dialysis patients [31-34]. This variation would be linked to the use of tools and different methodologies [35]. In our study, the prevalence of depression is 66 % in the whole population, and 80.4 % in the group of chronic pain sufferers, this finding is explained by the causal relationship between depression and chronic pain, several authors have proven that the causal link between chronic pain and depression is bilateral: chronic pain depresses the patient and this depression promotes chronic pain [36,37]. Besides depression, anxiety, is the most prevalent psychological factor associated with chronic pain [38]. A recent study places the prevalence of anxiety in chronic hemodialysis patients at 36.9 % [34], in our study, this rate represents 68 % for the entire population and 83.2 % in the group of chronic pain sufferers.

Studies have shown that anxiety about health is greater in people with pain than in the control group [39]. Along with these studies, many other studies have demonstrated the importance of psychological factors in the management of chronic pain [2]. In our study, the education level is retained also as a factor associated with chronic pain, people with little education are more likely to suffer from chronic pain than those with a higher level of education [1]. Indeed, an advanced level of education protects against chronic pain in hemodialysis patients, probably because of due to the cognitive skills that allow them to accept and manage their pain. These skills based on the level of education allow the patient to observe chronic pain, and understand it and thus to appropriate it [40]. Similarly, illiteracy is identified as a risk factor linked to chronic pain in hemodialysis [10].

The social status is also retained as a factor associated with chronic pain. Loneliness and social isolation increase the perception of chronic pain. Several studies confirm that being integrated into a social network provides support for the painful ordeal and promotes the reduction of the perceived chronic pain. Also, family support positively influences the patient’s behavioral and attitude responses to chronic pain. [40,41]. On the other way, disappointment in relation to the social support received, favors passive strategies for coping
with pain, increases the negative emotional response to pain; adjustment to chronic pain is therefore less good [38].

In our results, the fifth factor retained in multivariate analysis is marital status. Multiple studies have explored the potential association between marital status and chronic pain in hemodialysis patients [40-42]. One of these studies, found no correlation between pain and marital status [43], while the others confirmed that marital status is significantly associated with chronic pain on hemodialysis [40,41]. In our study, unmarried patients ultimately reported more chronic pain, similar to the work of Binik [43]. In fact, the understanding of the spouse and his real support are preponderant factors, for the chronic pain patient which condition, in a positive way, all his other behavioral responses and his attitudes towards pain [40].

STRENGTHS AND LIMITATIONS

Strengths of our study include its multi-center environment and relatively large sample size. It was also the first study in this region to assess chronic pain, examine its effect on the daily life of hemodialysis patients, and study the social, demographic, clinical and psychological factors associated with it. In addition, the current study used the BPI and HADS scales which are widely accepted assessment tools to study chronic pain symptoms and diagnose depression and anxiety, respectively, in hemodialysis patients. However, this study had some limitations,

The first is that the patients came from a single geographic region; It was conducted in a single population of hemodialysis patients and may not be generalizable to other hemodialysis populations. The second is that the cause of the pain has been determined just by examination of files and the last, is that the confidence intervals of the Odds rations are wide, it shows that the evaluation of the parameters is not so precise due to the size of the sample.

However, we believe that the results provide a solid basis for studies that will further explore this aspect. The ultimate goal should be a better understanding and treatment of chronic pain in hemodialysis patients.

CONCLUSION

Chronic pain on hemodialysis needs to be understood in the context of social, biological, psychological, and physical factors. A multidisciplinary approach is recommended for the management of complex pain syndromes, include both pharmacological and non-pharmacological interventions and that involves nurses, physiotherapists, occupational therapists, psychologists, health educators and family, to ensure a good quality of life for this vulnerable population of hemodialysis patients.

Pain assessment and management need to be incorporated into standard care for these patients. However, additional research is required to identify the most effective approaches to pain management for long-term hemodialysis patients.

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