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Complete List of Authors:	Marzouk, Mehdi; CHU F.Bourguiba, Intensive Care; Centre Hospitalier de Bethune, Nord pas-de-calais Ouanes-Besbes, Lamia; CHU F.Bourguiba Monastir, Intensive Care Med Ouanes, Islem; CHU Fattouma Bourguiba, ICU Dachraoui, Fahmi; CHU F.Bourguiba, Intensive Care Department Hammouda, Zeineb; CHU F.Bourguiba , Intensive Care Abroug, Fekri; CHU Fatouma Bourguiba, Intensive Care
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Prevalence of Anxiety and Depressive Symptoms among Medical Residents in Tunisia: A Cross-Sectional survey

Mehdi Marzouk[1] (MD),Lamia Ouanes-Besbes[1] (MD), Islem Ouanes[1] (MD), Fahmi Dachraoui[1] (MD), Zeineb Hammouda[1] (MD), Fekri Abroug[1] (MD)

Authors' affiliation :

[1] Intensive Care Department, Teaching Hospital, Fatouma Bourguiba ; 5000 Monastir. Tunisia

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Correspondence:

Fekri Abroug

Intensive Care Department

CHU F.Bourguiba. Monastir. 5000 Tunisia

f.abroug@rns.tn

Abstract:

Objective: assess the prevalence of anxiety and depressive symptoms in Tunisian residents and associated risk factors.

Design: cross-sectional survey

Setting: Faculty of Medicine, Tunis

Participants: all Tunisian residents willing to choose their next 6-month rotation

Intervention: the items of the Hospital Anxiety and Depression score (HAD) questionnaire was employed to capture the prevalence of anxiety and/or depression among residents. Statistical relationships between anxiety and depression, and socio-demographic and work-related data were explored by Poisson regression.

Results: 1,700 out of 2,200 (77%) medical residents (median age:28 years, female: 60.8%) answered the questionnaire. The median working hours per week were 60 [IQR: 48;76]; 73% ensured a median 6 [IQR: 4;7] night shifts per month; only 8% could benefit from compensatory rest. Overall, 74.1% of participating residents had either, definite (43.6%) or doubtful (30.5%) anxiety, while 62% had definite (30.5%) or doubtful (31.5%) depression symptoms, with 20% having both. Symptoms of anxiety-depression were significantly associated with resident's age (OR= 1.014; 95%CI:1.006-1.023, p= 0.001); female gender (OR= 1.114;95%CI: 1.083-1.145, p<0.0001); and the heavy burden of work imposed on a weekly or monthly basis, as reflected by night shift number per month (OR= 1.048;95%CI, 1.016-1.082, p= 0.03), worked hours per week (OR= 1.008;95%CI:1.005-1.011, p<0.0001). Compared to medical specialties, the generally accepted difficult specialties (surgical or medical-surgical) were associated with higher HAD scale (OR= 1.459;95%CI: 1.172-1.816, p= 0.001).

Conclusion: Tunisian residents experience a rate of anxiety/depression substantially higher than that reported at the international level. This phenomenon is worrying as it usually lasts beyond the residency years, and is also a source of an increase in medical errors, work dissatisfaction and attrition.

Strengths and limitations of this study:

- First study to assess the prevalence of Anxiety/Depression among Tunisian residents
- Provides insights into associated socio-demographic and work-related variables
- The large participation rate
- The HAD questionnaire is in French (but this language is well mastered by Tunisian residents)
- No information on the rates of moods disorders in the general Tunisian population for comparison
- No assessment of the prevalence of Burnout syndrome

The increasing exposure of physicians to stressful situations is a global phenomenon without distinction between age, sex, or level of advancement in the profession[1-4]. Only a few variables inherent in the personalities, or in work-related strain, are able to modulate the expression of this stress by attenuating or exaggerating the generated mood disorders (anxiety, depression, burn out), and their impact on the personal and professional life[5 6]. These disorders may hamper the physician's professional performance by affecting the concentration at work, and the quality of provided healthcare services, and provoking conflicts with patients or their families, or with colleagues, [7-9]. They are also associated with a higher substance use and abuse, divorce, and even more suicidal ideations [9 10] [11]. Medical residents seem at increased risk of developing mental disorders [7 12-14]. A recent systematic review reported a 28.8% pooled prevalence of depression or depressive symptoms in medical residents, with a wide variation in the rate (20.9% and 43.2%) depending on the instrument used[15]. In countries with socio-economic conditions similar to those of Tunisia, the prevalence of depressive symptoms in medical residents ranges from 17% in India to 48% in Argentina[16-18]

Tunisia is a country that is currently experiencing major socio-economic and political mutations as a consequence of the so-called "Jasmine revolution" which was in 2011 the spark that ignited the whole region during the "Arabic spring". These mutations have particularly altered the relationship between the main body of the society and the medical profession, the latter being perceived by a large part of the population as a body of privileged, insufficiently empathic, and little concerned by the misfortunes of the population. The assaults against doctors, particularly in public hospitals and their emergency services, malpractice suits and prosecutions, are now very frequent, and are highly publicized on a daily basis on the various media in the country. Moreover, public hospitals experienced just after the revolution a sharp deterioration in the resources and staff made available, together with an alteration of their governance, which paralleled that of the public health sector. This situation has greatly frustrated the population, in particular the citizens who cannot afford the private medical sector and its large out-of-pocket costs.

Among the medical profession, the young Tunisian residents are considered the pillar of these public hospitals. Residents are the only physicians present at the hospital at night, on weekends, and on holidays.

Residents come to term of a long, demanding, and selective course of studies. The typical resident must have passed his baccalaureate among the first ranked ones, be among the "happy few" who enter the medical school after a draconian selection, and successfully undergo a final residency contest usually after 2 to 3 attempts (Annual pass rate = 25%). Aged at least 26, the resident faces the reality of the public hospital, where he is exposed to stress resulting from non-optimal exercise conditions: the need to meet his professional duties set by his supervisors, and the growing demand of the population.

We hypothesized that the combination of all of these unfavorable circumstances for professional fulfillment, should result in a high level of mood disorders in medical residents. We conducted a large cross-sectional survey to address the prevalence in Tunisian residents of anxiety and depressive symptoms and highlight associated risk factors.

Patients-Methods

Participants : In Tunisia, specialization in medicine takes place at the end of general medical studies accomplished in one of the 4 faculties of medicine in the country. Doctors who wish to specialize do so following a national contest, bringing together the candidates from the four faculties of medicine. This contest is very selective, and takes place over three days. It consists in more than 300 questions (multiple choice, short answer), covering separately each of the following areas: medical specialties, surgical specialties, and basic sciences. More than 1,500 candidates participate annually, for about 500 elected members, who are ranked consecutively in order of merit. The choice of the specialty is then made according to the rank of success in the contest, on a number of posts that is equal to the number of candidates, and distributed among all the medical specialties by quotas which are fixed according to the needs of the country in doctors practicing in medical specialties. The internship periods (of 6 months each) and their distribution between specialties, in order to validate a given specialty, are specified in advance by the college of each specialty. Every six months, all trainee residents in the country (more than 2,000) gather over ten days at the Faculty of Medicine of Tunis, the Tunisian capital, to choose the next 6-month rotation. Within the chosen specialty, the candidate chooses according to seniority first, and his classification in the corresponding level afterwards.

Protocol: The study protocol was approved by the local Institutional Review Board of Fatouma Bourguiba Teaching Hospital, Monastir (reference #2013/108). All the medical residents gathered at the faculty of medicine of Tunis, between December 14 and December 22, 2015 for the choice of the next 6 month-rotation, were invited to answer an anonymous, self-administered questionnaire. The questionnaire covers their civil and marital status, the specialty chosen, their level of advancement in the specialty (duration 4 years for medical specialties and 5 years for surgical specialties), and items of the Hospital Anxiety and Depression score (HAD) questionnaire. On this specific date, the first level residents were the new candidates of the very recent residency contest and for the record, the 2015 residency contest' results were published on 17th December 2015 just 48 hours before an irreversible choice, which engages for lifetime.

Each residency level includes a number of residents between 300 and 600 and the operation of choice begins at 9am and lasts until 5pm.

A resident of our unit (MM) waited at the exit of the choice' lecture room to distribute the questionnaire to the residents who accepted to participate anonymously after they had just finished their choice operation.

Measurements : The questionnaire explored three fields: socio-demographic data, work-related characteristics, and HAD score.

Socio-demographic information concerned the gender, age, marital status, number of dependent children if married or divorced.

Work-related characteristics included specialty, the level achieved so far in the specific curriculum of each specialty, the number of shifts per month, working hours per week, and the presence or not of compensatory rest. For the statistical analysis purpose, specialties were split into four groups according to their degree of difficulty: medical (example dermatology, pulmonology, rheumatology, fundamental specialties like histology, physiology etc…) ; medical and surgical (example: ophthalmology, gynecology-obstetrics, otorhinolaryngology etc…); difficult medical specialties (example: critical care medicine, emergency medicine, cardiolgy), and difficult surgical specialties (neurosurgery, cardiovascular surgery etc).

The survey tool used in our study was Hospital Anxiety and Depression score (HAD) scale that was developed by Zigmond & Snaith [19]**.** It is a brief questionnaire (containing 14 items), and was originally designed to detect emotional disturbances in non-psychiatric patients treated at hospital clinics. It is a self-report rating scale designed to measure both anxiety and depression. It consists of two subscales, each containing seven items on a 4-point Likert scale (ranging from 0-3). HAD is scored by summing the ratings for the 14 items to yield a total score, and by summing the ratings for the 7 items of each subscale to yield separate scores for anxiety and depression. Two cutoff scores are validated for detecting anxiety and depression, namely 8 for doubtful cases and 11 for actual cases.

The survey was written in French and self-completed by each resident who has agreed to participate in the study, the residents having a perfect mastery of French, the language in which all medical studies are carried out in Tunisia. The total for depression, anxiety subscales the whole HAD scale were calculated by a resident from our unit.

Statistical analysis :

The study design focused on determination of the number of residents who meet the criteria for anxiety and depression. Continuous parameters are expressed as medians and inter-Quartile Ranges (IQR). The dichotomous variables are expressed as numbers and percentages. Adjusted Odds Ratios (ORs) and 95% Confidence Intervals (CIs) for each variable were calculated.

Prevalence of anxiety and depression were calculated and correlated to socio-demographic and work-related characteristics. Chi-square tests were carried out to compare the prevalence of anxiety and depression between groups. Multivariable Poisson regression was used to assess risk factors associated with anxiety and depression cases.

p-values less than 0.05 were considered statistically significant. All statistical procedures were performed using IBM SPSS Statistics 21.0 software.

Results:

During the study-period corresponding to December 14th to December 22nd 2015, 1700 out of 2200 (77%) medical residents willingly answered the proposed questionnaire. They had a median age of 28 years [IQR: 27; 30] with a predominance of the female gender (60.8%); 40% were married, of whom 20% had at least one child (Table I).

Tunisian Residents from all levels and different specialties answered the survey. Residents declared they used to work for a median of 60 hours [IQR : 48 ; 76] per week. 73% (1239) among them ensured night shifts with a median number of 6 [IQR : 4 ; 7] per month; only 8% (98) of these could benefit from compensatory rest. (Table I).

The median HAD score amounted to 19 [IQR: 14 ; 23], split on the anxiety subscale (HAD-A) : 10 [IQR: 7 ; 12], and the depression subscale (HAD-B): 9 [IQR: 6 ; 11].

Overall, 742 (43.6%) residents reached the cut-off defining definite anxiety state (ie a score ≥11), and 519 (30.5%) reached the scale level defining definite depression. Out of these residents, 342 (20%) had both anxiety and depression. In the remaining, the prevalence of doubtful anxiety score (ie a score ≥8) was 30.5%, and that of doubtful depression was 31.5%.

Tables II and III depict the association between demographic and workload characteristics, and the occurrence of anxiety or depression, respectively.

Age, female gender (66.7% Vs. 56.2%, p < 0.0001) and marital status (42% Vs. 36.7%, p = 0.027) were significantly associated with definite cases of anxiety (HAD-A ≥ 11) compared to negative or doubtful ones (HAD-A < 11). The fifth level of residency course (13.9% vs. 9.7%, p = 0.009), and the choice of medical/surgical specialties (15.9% Vs. 10.8%, p = 0.002) were also significantly associated with anxiety. Medical specialties (45% Vs. 54.2%, p <0.0001) were on the contrary associated with a lower risk of developing anxiety symptoms (Table II).

For definite depressive cases (HAD-D ≥ 11) compared to negative and doubtful ones (HAD-D < 11), age, marital status (45.7% Vs. 36.2%, p <0.0001) were significantly different between the two groups. Moreover, difficult surgical specialties (22.9% Vs. 17.5%, p = 0.011) were significantly associated with depressive symptoms in contrast to medical specialties (44.7 Vs. 52.6%, p = 0.003) which were associated with lower depressive symptoms (Table III).

The number of shifts per month, and working hours per month were associated with both probable anxiety and depressive cases (Table II and III).

The Poisson regression analysis disclosed the following variables as associated with HAD score: age (OR = 1.014, 95% CI, 1.006-1.023, p = 0.001); female gender (OR = 1.114, 95% CI, 1.083-1.145, p <0.0001); night shift number per month (OR = 1.048, 95% CI, 1.016-1.082, p = 0.03), working hours per week (OR = 1.008, 95% CI, 1.005-1.011, p = <0.0001) . Compared with medical specialties, medico-surgical ones (OR = 1.459, 95% CI, 1.172-1.816, p = 0.001) were independently associated with higher HAD scale (fig 1).

Discussion

This large survey encompassing 1700 out of the 2200 Tunisian residents involved in the periodic process of choosing internship positions in their specialties, shows that 74.1% of them fulfilled the criteria of either definite (43.6%) or doubtful (30.5%) anxiety, while 62% of them had either definite (30.5%) or doubtful (31.5%) depression symptoms. In 20% there were both symptoms of anxiety and depression. Symptoms of anxiety-depression were significantly associated with age, female sex, and the heavy burden of work imposed on a weekly or monthly basis as reflected by the weekly working hours, the night-shift number per month, and the choice of a specialty generally accepted as a difficult one (surgical or medical-surgical specialty compared to medical specialty).

Of interest, the system of work revealed in this survey is very demanding, since the average working hours per week (60 hours), and the number of night shifts per month (6 on average regardless of the type of specialty) most often without compensatory rest, are extremely high.

Although, mood disorders and physician distress such as burnout syndrome, depression, and anxiety are admitted as both, more prevalent among caregivers compared to general population, and a devastating situation in this particular population, information about their prevalence in Tunisia is scarce, both in the general population and in physicians [5 20 21]. In this first survey on the subject in our country, we succeeded to enroll 77% of potentially concerned residents, yielding a picture that could be considered both large and accurate snapshot of the actual situation of a corporate representing the real backbone of the public health system in Tunisia. The use of the French version of the HAD questionnaire should not be considered as a potential bias, as medical studies are conducted in French which is perfectly mastered by all Tunisian residents.

Benchmarking the rates of moods disorders observed in young physicians with those prevailing in the general Tunisian population is not easy since we are unaware of studies assessing anxiety and depression rates among general Tunisian population, but international studies stressed the fact that residents usually have higher rates of depression than the general population [15 22]. Estimates of the prevalence of depression or depressive symptoms among resident physicians vary from 3% to 60%, whereas a recent meta-analysis yielded an overall pooled prevalence of depression or depressive symptoms of 28.8%

rendering the definite or doubtful diagnosis rate of depression observed in our study very high in comparison to the median rate at the international level[15].

Resident physicians share the same known causes of depression than the general population: physical health, lifestyle, marital status, history of previous depression, childhood, religiosity etc… They have in addition specific factors pertaining to the work organisation and the development of their career [4]. These risk-factors correspond to the difficulty of their specialty, postgraduate year, stress at work, current rotation difficulty, working hours, shift number etc…[4 15 23]. In our study the Poisson regression model disclosed the following items as statistically associated with the occurrence of anxiety-depression: age, female sex, practice of a specialty generally accepted as a difficult one, and the heavy burden of work imposed on a weekly or monthly basis as reflected by the weekly working hours, and the night-shift number per month. Most of these risk-factors have been reported elsewhere, or are intuitive, but it is their magnitude that makes the originality, and intrigue in our study

The occurrence of depression should be considered as a major event in the young physician career or even life. It is indeed about a long-lasting phenomenon, as it has been shown that once present, depression as well as burnout is prone to persist throughout the whole residency duration, or even beyond [24 25]. In a nationwide survey involving 3500 Canadian physicians, Sullivan et al reported that 55% found that medicine as a profession impacted negatively their family and personal life, whereas 65% reported that opportunities to change career despite dissatisfaction were limited [26]

Depression is also a source of decreased concentration at work, an increase in the rate of medical error, work dissatisfaction and conflicts, impaired sleep quality, and a greater propensity to attrition[7 27 28]. Hence, every effort aiming at improving the mental health of young physicians should be encouraged. This begins by acting on the risk factors associated with anxiety and depression in this specific population.

The resident physician should first be aware of the mental problem and seek help. We did not investigate whether the participating residents sought for or actually had psychological counseling, but we strongly believe that most did not. Residents' careers and the pace of work should also be better managed. Some measures could be immediate such as a

compensatory rest after the night shifts. Others require the restoration of trust with the population, a better governance of the health system, objectives that seem very difficult to achieve in the current political and social climate in the country.

***Legend Figure1*:** Risk Factors associated with Total HAD Score

Authors' contributions

Study Concept and design: MM and FA; Data Acquisition: MM; Analysis and interpretation of the data: MM, LOB, ZH, IO, FD, FA; All authors read and approved the final manuscript. MM and FA had full access to the data and take responsibility for its integrity and the accuracy of the analyses.

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Table I : Demographic and work characteristics of the study population (n=1700) :

Sex ratio (M/F)		667/1033
Age, med [IQR]		28 [27 ; 30]
Marital Status	**Single**, n(%)	1036 (61)
	Married, n(%)	655 (38.5)
	Divorced, n(%)	9 (0.5)
Number of Children	**Zero**, n(%)	343 (20.2)
	One, n(%)	235 (13.8)
	More than one, n(%)	86 (5.1)
Residency Level (year)	**I,** n(%)	320 (18.8)
	II, n(%)	410 (24.1)
	III, n(%)	434 (25.5)
	IV, n(%)	340 (20)
	V, n(%)	196 (11.5)
Specialty*	**Medical,** n(%)	854 (50.2)
	Medical and Surgical, n(%)	221 (13%)
	Hard Medical, n(%)	299 (17.6)
	Hard Surgical, n(%)	326 (19.2)
Night shifts per month, med [IQR]		6 [4 ; 7]
Working hours per week, med [IQR]		60 [48 ; 76]
Compensatory rest, n (%)		98 (5.7)

**Specialties were split into four categories according to everyday difficulties: medical (example dermatology, pulmonology, rheumatology, fundamental specialties like histology, physiology etc) ; medical and surgical (example: ophthalmology, gynecology-obstetrics, otorhinolaryngology etc); hard medical (example: critical care medicine, emergency medicine, cardiolgy), and hard surgical specialties (neurosurgery, cardiovascular surgery etc).*

Table II : *Demographic and workload characteristics and their association with anxiety :*

		No Anxiety	Definite Anxiety	
n (%)		958 (56.4)	742 (43.6)	
Age, *med [IQR]*		29 [28 ; 30]	29 [28 ; 30]	0.008
Gender				<0.0001
	Male	420 (43.8)	247 (33.3)	
	Female	538 (56.2)	495 (66.7)	
Marital Status				0.027
	Single	606 (63.3)	430 (58)	
	Married	352 (36.7)	312 (42)	
Level of Residency				0.005
	I	188 (19.6)	132 (17.8)	
	II	244 (25.5)	166 (22.4)	
	III	251 (26.2)	183 (24.7)	
	IV	182 (19)	158 (21.3)	
	V	93 (9.7)	103 (13.9)	
Specialty				0.018
	Medical	519 (54.2)	334 (45)	
	Medical and Surgical	103 (10.8)	118 (15.9)	
	Hard Surgical	181 (18.9)	145 (19.5)	
	Hard Medical	155 (16.2)	145 (19.5)	
Shifts/month, med [IQR]		5 [2;7]	6 [5;8]	<0.0001
Working Hours/week, med [IQR]		60 [40;72]	60 [50 ; 80]	<0.0001

Table III : *Demographic and workload characteristics and association with depression cases*

		No depression	Definite depression	
N (%)		1181 (69.5)	519 (30.5)	
Age, *med [IQR]*		29 [28;30]	29 [28 ; 30]	<0.0001
Gender				0.281
	Male	453 (38.4)	214 (41.2)	
	Female	728 (61.6)	305 (58.8)	
Marital Status				<0.0001
	Single	754 (63.8)	282 (54.3)	
	Married	427 (36.2)	237 (45.7)	
Level of Residency				<0.0001
	I	263 (22.3)	57 (11)	
	II	292 (24.7)	118 (22.7)	
	III	294 (24.9)	140 (27)	
	IV	218 (18.5)	122 (23.5)	
	V	114 (9.7)	82 (15.8)	
Specialty				0.962
	Medical	621 (52.6)	232 (44.7)	
	Medical and Surgical	156 (13.2)	65 (12.5)	
	Hard Surgical	207 (17.5)	119 (22.9)	
	Hard Medical	197 (16.7)	103 (19.8)	
Shifts/month, *med [IQR]*		5 [3;7]	6 [4 ; 8]	<0.0001
Working Hours/week, *med [IQR]*		60 [42;72]	64 [51 ; 80]	<0.0001

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation	
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	X
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	X
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	P3
Objectives	3	State specific objectives, including any prespecified hypotheses	P4
Methods			
Study design	4	Present key elements of study design early in the paper	P5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	P5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	P5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	P5
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	P6
Bias	9	Describe any efforts to address potential sources of bias	P5
Study size	10	Explain how the study size was arrived at	P5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	P7
		(*b*) Describe any methods used to examine subgroups and interactions	NA
		(*c*) Explain how missing data were addressed	NA
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	NA
		(*e*) Describe any sensitivity analyses	P7
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	P8
		(b) Give reasons for non-participation at each stage	P8
		(c) Consider use of a flow diagram	NA
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	TableI
		(b) Indicate number of participants with missing data for each variable of interest	NA
Outcome data	15*	Report numbers of outcome events or summary measures	P8
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	P8

		(*b*) Report category boundaries when continuous variables were categorized	P8
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	NA
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	P8
Discussion			
Key results	18	Summarise key results with reference to study objectives	P10
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	P10
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	P10-11
Generalisability	21	Discuss the generalisability (external validity) of the study results	P11
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	P1

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Prevalence of Anxiety and Depressive Symptoms among Medical Residents in Tunisia: A Cross-Sectional survey

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Prevalence of Anxiety and Depressive Symptoms among Medical Residents in Tunisia: A Cross-Sectional survey

Mehdi Marzouk[1] (MD),Lamia Ouanes-Besbes[1] (MD), Islem Ouanes[1] (MD), Zeineb Hammouda[1] (MD), Fahmi Dachraoui[1] (MD), Fekri Abroug[1] (MD)

Authors' affiliation :

[1] Intensive Care Department, Teaching Hospital, Fatouma Bourguiba and Research Laboratory (LR12SP15), University of Monastir; 5000 Monastir. Tunisia

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Correspondence:

Fekri Abroug

Intensive Care Department

CHU F.Bourguiba. Monastir. 5000 Tunisia

f.abroug@rns.tn

Abstract:

Objective: assess the prevalence of anxiety and depressive symptoms, and associated risk factors in Tunisian residents.

Design: cross-sectional survey

Setting: Faculty of Medicine, Tunis

Participants: all Tunisian residents brought together to choose their next 6-month rotation

Intervention: the items of the Hospital Anxiety and Depression score (HAD) questionnaire was employed to capture the prevalence of anxiety and/or depression among residents. Statistical relationships between anxiety and depression, and socio-demographic and work-related data were explored by Poisson regression.

Results: 1,700 out of 2,200 (77%) medical residents (mean age: 28.5±2 years, female: 60.8%) answered the questionnaire. The mean working hours per week were 62±21 hours; 73% ensured a mean of 5.4±3 night shifts per month; only 8% of them could benefit from a day of safety rest. Overall, 74.1% of participating residents had either, definite (43.6%) or doubtful (30.5%) anxiety, while 62% had definite (30.5%) or doubtful (31.5%) depression symptoms, with 20% having both. Symptoms of anxiety-depression were significantly associated with resident's age (OR= 1.014; 95%CI:1.006-1.023, p= 0.001); female gender (OR= 1.114;95%CI: 1.083-1.145, p<0.0001); and the heavy burden of work imposed on a weekly or monthly basis, as reflected by night shift number per month (OR= 1.048;95%CI, 1.016-1.082, p= 0.03), worked hours per week (OR= 1.008;95%CI:1.005-1.011, p<0.0001). Compared to medical specialties, the generally accepted difficult specialties (surgical or medical-surgical) were associated with higher HAD scale (OR= 1.459;95%CI: 1.172-1.816, p= 0.001).

Conclusion: Tunisian residents experience a rate of anxiety/depression substantially higher than that reported at the international level. This phenomenon is worrying as it has been associated with an increase in medical errors, work dissatisfaction and attrition. Means of improving the well-being of Tunisian residents are explored, emphasizing those requiring immediate implementation.

Strengths and limitations of this study:

- First study to assess the prevalence of Anxiety/Depression among Tunisian residents
- The large participation rate
- The HAD questionnaire is in French (but this language is well mastered by Tunisian residents)
- No information on the rates of mood disorders in the general Tunisian population for comparison
- No assessment of the prevalence of Burnout syndrome

Physicians are increasingly exposed to stressful situations regardless of age, gender, or seniority in the profession[1-4]. Only a few variables inherent in the personalities, or in work-related strain, are able to modulate the expression of this stress by attenuating or exaggerating the generated mood disorders (anxiety, depression, burn out), and their impact on the personal and professional life[5 6]. These disorders may hamper the physician's professional performance by affecting the concentration at work, and the quality of provided healthcare services, and provoking conflicts with patients or their families, or with colleagues, [7-9]. They are also associated with a higher substance use and abuse, divorce, and even more suicidal ideations [9 10 11]. Medical residents seem at increased risk of developing mental disorders [7 12-14]. A recent systematic review reported a 28.8% pooled prevalence of depression or depressive symptoms in medical residents with a wide variation in this rate, depending on the instrument used[15]. In countries with socio-economic conditions similar to those of Tunisia, the prevalence of depressive symptoms in medical residents ranges from 17% in India to 48% in Argentina [16-18]

Tunisia is a country that is currently experiencing major socio-economic and political changes as a consequence of "Arab spring". Arab spring was a series of anti-government protests, or armed rebellions ignited in Tunisia by the so-called "Jasmine revolution" which spread across North African countries and in the Middle East. It is seen as the translation of peoples' aspirations to democracy, and to replace dictators in place. According to the United nations Development Program (UNDP), the average annual Human Development Index (HDI) has fallen in Tunisia from 0.88% during the decade before the advent of the Arab spring to 0.25% during the 5 years that followed leading to a sustained erosion of the middle class, an increase in poverty, and a decrease in overall wealth[19]. The Tunisian downturn has particularly altered the relationship between the main body of the society and the medical profession, the latter being perceived by a large part of the population as a body of privileged, insufficiently empathic, and little concerned by the misfortunes of the population. The assaults against doctors, particularly in public hospitals and their emergency services, malpractice suits and prosecutions, are now very frequent, and are highly publicized on a daily basis on the various media in the country. Moreover, public hospitals experienced just after the revolution a sharp deterioration in the resources and staff made available, together with an alteration of their governance, which paralleled that of the public health sector[20].

This situation has greatly frustrated the population, in particular the citizens who cannot afford the private medical sector and its large out-of-pocket costs[21].

Among the medical profession, the young Tunisian residents are considered the pillar of these public hospitals. Residents are the only physicians present at the hospital at night, on weekends, and on holidays.

Residents come to term of a long, demanding, and selective course of studies. The typical resident must have passed his baccalaureate among the first ranked ones, be among the "happy few" who enter the medical school after a tight selection. Indeed, admission to one of the four Faculties of Medicine is reserved to top-ranked graduates both in the baccalaureate and in a specific ranking taking into account the grades of key scientific disciplines. Overall, only 3 to 5% of bachelors are accepted annually to pursue medical studies. After 7 years of medical studies, graduates wishing to specialize, have to successfully undergo a final residency contest usually after 2 to 3 attempts (Annual pass rate = 25%). Aged at least 26, the resident faces the reality of the public hospital, where he is exposed to stress resulting from non-optimal working conditions: the need to meet his professional duties set by his supervisors, and the growing demand of the population.

We hypothesized that the combination of all of these unfavorable circumstances for professional fulfillment, should result in a high level of mood disorders in medical residents. We conducted a large cross-sectional survey to address the prevalence in Tunisian residents of anxiety and depressive symptoms and highlight associated risk factors.

Patients-Methods

Participants : In Tunisia, specialization in medicine takes place at the end of general medical studies accomplished in one of the four faculties of medicine in the country. Doctors who wish to specialize do so following a national contest, bringing together the candidates from the four faculties of medicine. This contest is very selective, and takes place over three days. It consists in more than 300 questions (multiple choice, short answer), covering separately each of the following areas: medical specialties, surgical specialties, and basic sciences. More than 1,500 candidates participate annually, for about 500 elected members, who are ranked consecutively in order of merit. The choice of the specialty is then made according to the rank of success in the contest, on a number of posts that is equal to the number of candidates, and distributed among all the medical specialties by quotas which are fixed according to the needs of the country in doctors practicing in medical specialties. The internship periods (of 6 months each) and their distribution between specialties, in order to validate a given specialty, are specified in advance by the college of each specialty. Every six months, all trainee residents in the country (more than 2,000) gather over ten days at the Faculty of Medicine of Tunis, the Tunisian capital, to choose the next 6-month rotation. Within the chosen specialty, the candidate chooses according to seniority first, and his classification in the corresponding level afterwards.

Protocol: The study protocol was approved by the local Institutional Review Board of Fatouma Bourguiba Teaching Hospital, Monastir (reference #2013/108). All the medical residents gathered at the faculty of medicine of Tunis, between December 14 and December 22, 2015 for the choice of the next 6 month-rotation, were invited to answer an anonymous, self-administered questionnaire. The questionnaire covers their civil and marital status, the specialty chosen, their level of advancement in the specialty (duration 4 years for medical specialties and 5 years for surgical specialties), and items of the Hospital Anxiety and Depression score (HAD) questionnaire[22].

Each residency level includes 300-600 young physicians whose order of passage depends on their ranking. Participants answered the questionnaire immediately after having made their choice.

Measurements : The questionnaire explored three fields: socio-demographic data, work-related characteristics, and HAD score.

Socio-demographic information concerned the gender, age, marital status, number of dependent children if married or divorced.

Work-related characteristics included specialty, the level achieved so far in the specific curriculum of each specialty, the number of shifts per month, whether the shift is followed by a day of safety rest, and total working hours per week. For the statistical analysis purpose, specialties were split into four groups according to the associated workload: medical (example dermatology, pulmonology, rheumatology, psychiatry, fundamental specialties such as histology, physiology etc…) ; medical and surgical (example: ophthalmology, gynecology-obstetrics, otorhinolaryngology etc…); medical specialties with high workload (example: critical care medicine, emergency medicine, cardiology), and surgical specialties with high workload (neurosurgery, cardiovascular surgery etc).

The survey tool used in our study was Hospital Anxiety and Depression score (HAD) scale that was developed by Zigmond & Snaith [22]**.** It is a brief questionnaire (containing 14 items), and was originally designed to detect emotional disturbances in non-psychiatric patients treated at hospital clinics. It is a self-report rating scale designed to measure both anxiety and depression. It consists of two subscales, each containing seven items on a 4-point Likert scale (ranging from 0-3). Participants were told that the questions asked relate to their psychic state during the last two weeks. HAD is scored by summing the ratings for the 14 items to yield a total score, and by summing the ratings for the 7 items of each subscale to yield separate scores for anxiety and depression. Two cutoff scores are validated for detecting anxiety and depression, namely 11 for participants who screen positive for anxiety/depression and 8 for probable anxiety/depression.

The survey was written in French and self-completed by each resident who has agreed to participate in the study. The language of the survey is not actually a barrier to the residents' completion of the survey, because that is the language of all medical studies in the country. The total for depression, anxiety subscales the whole HAD scale were calculated by a resident from our unit**.**

Statistical analysis :

The study design focused on determination of the number of residents who meet the criteria for anxiety and depression. Continuous variables are expressed either as means ± Standard Deviations or medians and inter-Quartile Ranges (IQR), according to normal or skewed data distribution. The dichotomous variables are expressed as numbers and percentages. Adjusted Odds Ratios (ORs) and 95% Confidence Intervals (CIs) for each variable were calculated.

Prevalence of anxiety and depression were calculated and correlated to socio-demographic and work-related characteristics. Chi-square tests were carried out to compare the prevalence of anxiety and depression between groups. Multivariable Poisson regression was used to assess risk factors associated with anxiety and depression cases.

Statistical significance was denoted by ***p***-values less than 0.05. All statistical procedures were performed using IBM SPSS Statistics 21.0 software.

Participants and Public involvement: No participants were involved in setting the research question or in the design or conduct of the study. No participants were asked to advise on interpretation or writing up of results. There are no plans to disseminate the results of the research individually to study participants.

Results:

During the study-period corresponding to December 14th to December 22nd 2015, 1700 out of 2200 (77%) medical residents from all levels and different specialties answered the survey. They had a mean (±SD) age of 28.5±2 years with a predominance of the female gender (60.8%); 38.5% were married, of whom 19% had at least one child (Table I).

Residents declared they used to work for a mean of 62±21 hours per week; 73% (1239) among them ensured night shifts with a mean number of 5.4±3 per month, of whom only 8% (98) declared that the shift was systematically followed by a day of safety rest (Table I).

The median HAD score amounted to 19 [IQR: 14 ; 23], split on the anxiety subscale (HAD-A) : 10 [IQR: 7 ; 12], and the depression subscale (HAD-B): 9 [IQR: 6 ; 11].

Overall, 742 (43.6%) residents reached the cut-off defining definite anxiety state (ie a score ≥11), and 519 (30.5%) reached the scale level defining definite depression. Out of these residents, 342 (20%) had both anxiety and depression. In the remaining, the prevalence of doubtful anxiety score (ie a score ≥8) was 30.5%, and that of doubtful depression was 31.5%.

Tables II and III depict the association between demographic and workload characteristics, and the occurrence of anxiety or depression, respectively.

Univariate analysis disclosed age, female gender (66.7% Vs. 56.2%, $p < 0.0001$) and marital status (42% Vs. 36.7%, $p = 0.027$) as significantly associated with definite cases of anxiety (HAD-A ≥ 11) compared to negative or doubtful ones (HAD-A < 11). The fifth level of residency course (13.9% vs. 9.7%, $p = 0.009$), and the choice of medical/surgical specialties (15.9% Vs. 10.8%, $p = 0.018$) were also significantly associated with anxiety. Medical specialties (45% Vs. 54.2%, $p <0.0001$) were on the contrary associated with a lower risk of developing anxiety symptoms (Table II).

For definite depressive cases (HAD-D ≥ 11) compared to negative and doubtful ones (HAD-D < 11), age, marital status (45.7% Vs. 36.2%, $p <0.0001$) were significantly different between the two groups. Moreover, surgical specialties associated with high-workload (22.9% Vs. 17.5%, $p = 0.011$) were significantly associated with depressive symptoms in contrast to medical specialties (44.7 Vs. 52.6%, $p = 0.003$) which were associated with lower depressive symptoms (Table III).

The number of shifts per month, and working hours per month were associated with both anxiety and depressive cases (Table II and III).

The Poisson regression analysis disclosed the following variables as associated with HAD score: age (OR = 1.014, 95% CI, 1.006-1.023, p = 0.001); female gender (OR = 1.114, 95% CI, 1.083-1.145, p <0.0001); night shift number per month (OR = 1.048, 95% CI, 1.016-1.082, p = 0.03), working hours per week (OR = 1.008, 95% CI, 1.005-1.011, p = <0.0001) . Compared with medical specialties, medico-surgical ones were independently associated with higher HAD scale (OR = 1.459, 95% CI, 1.172-1.816, p = 0.001; fig 1).

Discussion

This large survey encompassing 1700 out of the 2200 Tunisian residents brought together for the periodic process of choosing internship positions in their specialties, shows that 43.6% of them had definite criteria of anxiety, and 30.5% had depression. The diagnosis of anxiety or depression was doubtful in an additional 30% each. Symptoms of anxiety-depression were significantly associated with age, female sex, and the heavy burden of work imposed on a weekly or monthly basis as reflected by the high number of weekly working hours, the night-shift number per month, and the choice of a specialty generally accepted as a difficult one (surgical or medical-surgical specialty compared to medical specialty).

Of interest, this survey unveils a very demanding health system imposed to Tunisian residents as reflected by the average working hours per week (60 hours), and the number of night shifts per month (6 on average regardless of the type of specialty), most often without a day of safety rest.

Although, mood disorders and physician distress (such as burnout and depression) are more prevalent among medical professionals compared to general population, information is lacking about their prevalence in Tunisia [5 23 24]. This first survey on the subject in our country, enrolled 77% of potentially concerned residents, yielding a snapshot on the burden incurred by residents from all specialties in their everyday practice. The use of the French version of the HAD questionnaire should not be considered as a barrier to the residents' completion of the survey, because that is the language of all medical studies in the country.

International studies stressed the fact that residents usually have higher rates of depression than the general population[15 25]. Estimates of the prevalence of depression or depressive symptoms among resident physicians vary from 3% to 60% with a median of 28.8% according to a recent meta-analysis of 54 studies, a proportion that is lower than that recorded in our study whether we only consider the rate of definite depression, or when we add the additional cases qualifying for doubtful depression[15]. Of interest, this meta-analysis emphasized the difference in the methodological approach to address this issue (cross sectional vs longitudinal studies), and the great variability in the instruments used (no less than 13 different instruments used in the 54 studies)[15]. A prospective cohort study conducted in Switzerland and using the HAD inventory used in our study disclosed a prevalence of 30% anxiety symptoms in the second year residents, and 20% in the fourth

and sixth year residents; depression symptoms were present in 15% and 10%, respectively[26]. However, benchmarking with countries with socio-economic similarities could be more insightful. In a study including 118 residents from the American University of Beirut, 22% qualified for moderate to major depressive symptoms while only 8% had anxiety[27]. Moreover, in a cross sectional study conducted among residents of various specialties in Saudi Arabia, the prevalence of moderate to severe depressive symptoms was around 20% [17].

Resident physicians share the same known causes of depression than the general population: physical health, lifestyle, marital status, history of previous depression, childhood, religiosity etc… They have in addition specific factors according to the way the work is done, its everyday planning, and the constraints inherent to their career development [4]. These risk-factors correspond to the difficulty of their specialty, postgraduate year, stress at work, current rotation difficulty, working hours, shift number etc…[4 15 28]. In our study the Poisson regression model disclosed the following items as statistically associated with the occurrence of anxiety-depression: age, female sex, practice of a specialty generally accepted as very demanding and difficult, and the heavy burden of work imposed on a weekly or monthly basis as reflected by the weekly working hours, and the night-shift number per month. Most of these risk-factors have been reported elsewhere, or are intuitive, but it is their magnitude that makes this study important.

The occurrence of depression should be considered as a major event in the young physician career or even life. It has been shown that once present, depression as well as burnout may persist throughout the whole residency duration, or even beyond [29 30]. In a nationwide survey involving 3500 Canadian physicians, Sullivan et al reported that 55% found that medicine as a profession impacted negatively on their family and personal life, whereas 65% reported that opportunities to change career despite dissatisfaction were limited [31]. Depression is also a source of decreased concentration at work, an increase in the rate of medical error, work dissatisfaction and conflicts, impaired sleep quality, and a greater propensity to attrition, and even suicide ideation [7 32 33].

Considering the high prevalence of anxiety and depression among Tunisian medical residents, every effort aiming at improving the mental health of young physicians should be encouraged. Any strategy should target both the personal level to amend the identified and

potentially actionable risk-factors, and include more measures targeting the general organization of residents' work modalities, and their relationship with the hierarchy and administration.

The resident physician should first be aware of the mental problem and seek help in particular those with previous personal history of depression[34]. We did not investigate whether the participating residents sought for, or actually had psychological counseling, but we strongly believe that most did not. More generally, accepted risk factors such as age, gender, marital status, stressors outside work, sleep deprivation, or lifestyle, require more personal attention[4]. The current study was not designed to allow participants' identification so that they could be given individual information and act on it. Future studies targeting preferentially residents (or specialties) at high risk of anxiety, depression, or burnout, should consider such feedback for more specific training programs.

Residency program factors and the pace of work should also be better managed. While these details were totally non-existent in Tunisia, this has been recently defined through the promulgation on March 9, 2018 of the bylaw regarding the status of Tunisian interns and residents[35]. This promulgation, which has been obtained following long negotiations, and a strike that lasted more than 6 weeks, defines for the first time the role and duty of residents. The maximum number of weekly working hours and that of shift frequency have been clearly defined and have been reduced to a maximum of 40 hours and two per week, respectively. A day of safety rest following every shift has been rendered mandatory. Although still debated, the issue of work-hour restriction could be effective in reducing high emotional exhaustion despite the fact that it carries the risk of alteration in the quality of care and education[36].

Table I : Demographic and work characteristics of the study population (n=1700) :

Sex ratio (M/F)		667/1033
Age, med [IQR]		28 [27 ; 30]
Marital Status	**Single**, n(%)	1036 (61)
	Married, n(%)	655 (38.5)
	Divorced, n(%)	9 (0.5)
Number of Children	**Zero**, n(%)	343 (20.2)
	One, n(%)	235 (13.8)
	More than one, n(%)	86 (5.1)
Residency Level (year)	**I,** n(%)	320 (18.8)
	II, n(%)	410 (24.1)
	III, n(%)	434 (25.5)
	IV, n(%)	340 (20)
	V, n(%)	196 (11.5)
Specialty*	**Medical,** n(%)	854 (50.2)
	Medical and Surgical, n(%)	221 (13%)
	High-workload Medical specialties, n(%)	299 (17.6)
	High-workload Surgical specialties, n(%)	326 (19.2)
Working hours per week, med [IQR]		60 [48 ; 76]
Night shifts per month, med [IQR]		6 [4 ; 7]
Recovery day following night shift, n (%)		98 (8)

**Specialties were split into four categories according to everyday difficulties: medical (example dermatology, pulmonology, rheumatology, neurology, psychiatry, fundamental specialties like histology, physiology etc) ; medical and surgical (example: ophthalmology, gynecology-obstetrics, otorhinolaryngology etc); high-workload medical (example: critical care medicine, anesthesiology, emergency medicine, cardiolgy), and high-workload surgical specialties (surgery, pediatric surgery, orthopedics, neurosurgery, urology, cardiovascular surgery etc).*

Table II : *Demographic and workload characteristics and their association with anxiety :*

		No Anxiety	Definite Anxiety	*p*
n (%)		958 (56.4)	742 (43.6)	
Age, *mean±SD*		28.5±1.9	28.7±2	**0.008**
Gender				**0.0001**
	Male	420 (43.8)	247 (33.3)	
	Female	538 (56.2)	495 (66.7)	
Marital Status				**0.027**
	Single	606 (63.3)	430 (58)	
	Married	352 (36.7)	312 (42)	
Level of Residency				**0.005**
	I	188 (19.6)	132 (17.8)	
	II	244 (25.5)	166 (22.4)	
	III	251 (26.2)	183 (24.7)	
	IV	182 (19)	158 (21.3)	
	V	93 (9.7)	103 (13.9)	
Specialty				**0.018**
	Medical	519 (54.2)	334 (45)	
	Medical and Surgical	103 (10.8)	118 (15.9)	
	High-workload Surgical specialties	181 (18.9)	145 (19.5)	
	High-workload Medical specialties	155 (16.2)	145 (19.5)	
Shifts/month, *mean±SD*		4.9±3	6±2.9	**0.0001**
Working Hours/week, *mean±SD*		58.8±20	66.4±20	**0.0001**

Table III : *Demographic and workload characteristics and association with depression cases*

		No depression	Definite depression	*p*
N (%)		1181 (69.5)	519 (30.5)	
Age, *mean±SD*		28.3±1.8]	29±2	**0.007**
Gender				0.11
	Male	453 (38.4)	214 (41.2)	
	Female	728 (61.6)	305 (58.8)	
Marital Status				**0.0001**
	Single	754 (63.8)	282 (54.3)	
	Married	427 (36.2)	237 (45.7)	
Level of Residency				**0.0001**
	I	263 (22.3)	57 (11)	
	II	292 (24.7)	118 (22.7)	
	III	294 (24.9)	140 (27)	
	IV	218 (18.5)	122 (23.5)	
	V	114 (9.7)	82 (15.8)	
Specialty				**0.006**
	Medical	621 (52.6)	232 (44.7)	
	Medical and Surgical	156 (13.2)	65 (12.5)	
	High-workload Surgical specialties	207 (17.5)	119 (22.9)	
	High-workload Medical specialties	197 (16.7)	103 (19.8)	
Shifts/month, *mean±SD]*		5±3	6±2.9	**0.0001**
Working Hours/week, *med [IQR]*		60±20	66±20	**0.0001**

***Legend Figure1*:** Risk Factors associated with Total HAD Score

Authors' contributions

Study Concept and design: MM and FA; Data Acquisition: MM; Analysis and interpretation of the data: MM, LOB, ZH, IO, FD, FA; All authors read and approved the final manuscript. MM and FA had full access to the data and take responsibility for its integrity and the accuracy of the analyses.

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Data Sharing statement: dataset is available by contacting FA at f.abroug@rns.tn

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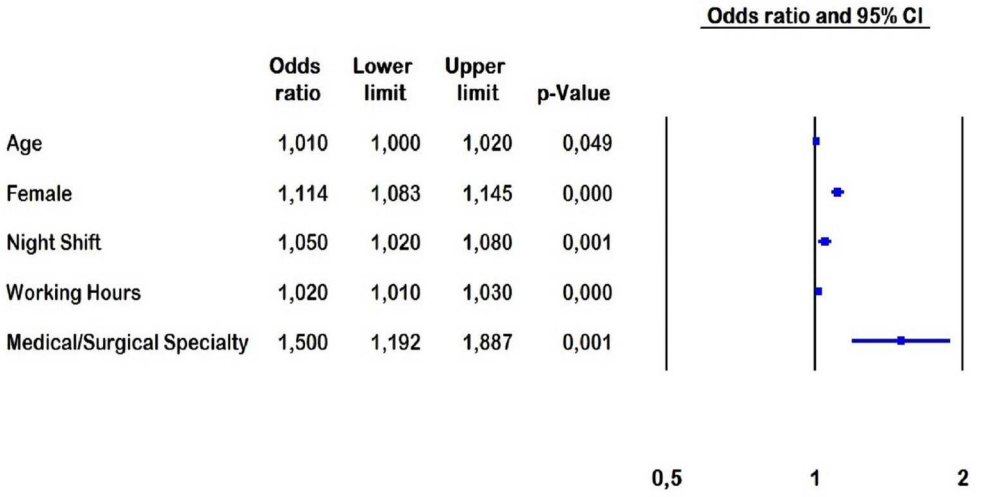

Risk factors for Anxiety/depression

541x304mm (96 x 96 DPI)

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation	
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	X
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	X
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	P2
Objectives	3	State specific objectives, including any prespecified hypotheses	P2
Methods			
Study design	4	Present key elements of study design early in the paper	P5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	P5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	P5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	P6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	P6
Bias	9	Describe any efforts to address potential sources of bias	P6
Study size	10	Explain how the study size was arrived at	P7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	P7
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	P7
		(*b*) Describe any methods used to examine subgroups and interactions	NA
		(*c*) Explain how missing data were addressed	P7
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	NA
		(*e*) Describe any sensitivity analyses	P7
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	P8
		(b) Give reasons for non-participation at each stage	P8
		(c) Consider use of a flow diagram	NA
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	TableI
		(b) Indicate number of participants with missing data for each variable of interest	NA
Outcome data	15*	Report numbers of outcome events or summary measures	P8
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	P8

		(*b*) Report category boundaries when continuous variables were categorized	P8
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	NA
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	P9
Discussion			
Key results	18	Summarise key results with reference to study objectives	P10
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	P10
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	P10-11
Generalisability	21	Discuss the generalisability (external validity) of the study results	P11
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	P1

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Prevalence of Anxiety and Depressive Symptoms among Medical Residents in Tunisia: A Cross-Sectional survey

Mehdi Marzouk[1] (MD),Lamia Ouanes-Besbes[1] (MD), Islem Ouanes[1] (MD), Zeineb Hammouda[1] (MD), Fahmi Dachraoui[1] (MD), Fekri Abroug[1] (MD)

Authors' affiliation :

[1] Intensive Care Department, Teaching Hospital, Fatouma Bourguiba and Research Laboratory (LR12SP15), University of Monastir; 5000 Monastir. Tunisia

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Correspondence:

Fekri Abroug

Intensive Care Department

CHU F.Bourguiba. Monastir. 5000 Tunisia

f.abroug@rns.tn

Abstract:

Objective: assess the prevalence of anxiety and depressive symptoms, and associated risk factors in Tunisian medical residents.

Design: cross-sectional survey

Setting: Faculty of Medicine, Tunis

Participants: all Tunisian medical residents brought together between December 14 and 22, 2015, to choose their next 6-month rotation

Intervention: the items of the Hospital Anxiety and Depression score (HAD) questionnaire was employed to capture the prevalence of anxiety and/or depression among residents. Statistical relationships between anxiety and depression (HAD score), and socio-demographic and work-related data were explored by Poisson regression.

Results: 1,700 out of 2,200 (77%) medical residents (mean age: 28.5±2 years, female: 60.8%) answered the questionnaire. The mean working hours per week were 62±21 hours; 73% ensured a mean of 5.4±3 night shifts per month; only 8% of them could benefit from a day of safety rest. Overall, 74.1% of participating residents had either, definite (43.6%) or probable (30.5%) anxiety, while 62% had definite (30.5%) or probable (31.5%) depression symptoms, with 20% having both definite anxiety and definite depression. Total HAD score was significantly associated with resident's age (OR=1.014; 95%CI:1.006-1.023, p=0.001); female gender (OR=1.114;95%CI: 1.083-1.145, p<0.0001); and the heavy burden of work imposed on a weekly or monthly basis, as reflected by night shift number per month (OR=1.048;95%CI, 1.016-1.082, p=0.03), worked hours per week (OR=1.008;95%CI:1.005-1.011, p<0.0001). Compared to medical specialties, the generally accepted difficult specialties (surgical or medical-surgical) were associated with a higher HAD score (OR=1.459;95%CI: 1.172-1.816, p=0.001).

Conclusion: Tunisian residents experience a rate of anxiety/depression substantially higher than that reported at the international level. This phenomenon is worrying as it has been associated with an increase in medical errors, work dissatisfaction and attrition. Means of improving the well-being of Tunisian medical residents are explored, emphasizing those requiring immediate implementation.

Strengths and limitations of this study:

- First study to assess the prevalence of Anxiety/Depression among Tunisian residents
- The large participation rate
- The HAD questionnaire is in French (but this language is well mastered by Tunisian residents)
- No information on the rates of mood disorders in the general Tunisian population for comparison
- No assessment of the prevalence of Burnout syndrome

Physicians are increasingly exposed to stressful situations regardless of age, gender, or seniority in the profession[1-4]. Only a few variables inherent in the personalities, or in work-related strain, are able to modulate the expression of this stress by attenuating or exaggerating the generated mood disorders (anxiety, depression, burnout), and their impact on the personal and professional life[5 6]. Medical residents seem at increased risk of developing mental disorders [7-10]. These disorders may hamper the physician's professional performance by affecting their concentration at work, and the quality of provided healthcare services, and provoking conflicts with patients or their families, or with colleagues, [9 11 12]. These mental health issues are also associated with a higher substance use and abuse, divorce, and even more suicidal ideations [12 13 14]. A recent systematic review reported a 28.8% pooled prevalence of depression or depressive symptoms in medical residents with a wide variation in this rate, depending on the instrument used[15]. In countries with socio-economic conditions similar to those of Tunisia, the prevalence of depressive symptoms in medical residents ranges from 17% in India to 48% in Argentina [16-18]

Tunisia is a country that is currently experiencing major socio-economic and political changes as a consequence of "Arab spring". Arab spring was a series of anti-government protests, or armed rebellions ignited in Tunisia by the so-called "Jasmine revolution" which spread across North African countries and in the Middle East. It is seen as the translation of peoples' aspirations to democracy, and to replace dictators in place. According to the United nations Development Program (UNDP), the average annual Human Development Index (HDI) has fallen in Tunisia from 0.88%, during the decade before the advent of the Arab spring, to 0.25% during the 5 years that followed. This lead to a sustained erosion of the middle class, an increase in poverty, and a decrease in overall wealth[19]. The Tunisian downturn has particularly altered the relationship between the main body of the society and the medical profession, the latter being perceived by a large part of the population as a body of privileged, insufficiently empathic, with little concern for the misfortunes of the population. Assaults against doctors, particularly in public hospitals and their emergency services, malpractice suits and prosecutions, are now very frequent, and are highly publicized on a daily basis by the various media in the country. Just after the revolution, public hospitals experienced a sharp deterioration in the resources and staff made available, together with an alteration in their governance[20]. This situation has greatly frustrated the population, in

particular the citizens who cannot afford the private medical sector and its large out-of-pocket costs[21].

Residents come to term of a long, demanding, and selective course of studies. The typical resident must have passed his baccalaureate among the first ranked ones, be among the "happy few" (3-5% top-ranked graduates) who enter to one of the four Tunisian medical schools. After 7 years of medical studies, graduates wishing to specialize, have to successfully undergo a final residency contest. Success usually takes 2 to 3 attempts (annual pass rate = 25%). Aged at least 26, the medical resident faces the reality of the public hospital where residents are the only physicians present in the hospital at night, on weekends, and on holidays. They are also exposed to stress resulting from non-optimal working conditions: the need to meet professional duties set by supervisors, and the growing demand of the population.

We hypothesized that the combination of all of these unfavorable circumstances for professional fulfillment, should result in a high level of mood disorders in medical residents. We conducted a large cross-sectional survey to address the prevalence of anxiety and depressive symptoms and associated risk factors in Tunisian medical residents.

Patients-Methods

Participants : In Tunisia, specialization in medicine takes place at the end of general medical studies. Doctors who wish to specialize do so following a national contest, bringing together the candidates from the four faculties of medicine. This contest is very selective, and takes place over three days. It consists of more than 300 questions (multiple choice, short answer), covering separately each of the following areas: medical specialties, surgical specialties, and basic sciences.

More than 1,500 candidates participate annually, for about 500 elected members, who are ranked consecutively in order of merit. The choice of the specialty is then made according to the rank of success in the contest, on a number of places that is equal to the number of candidates. Distribution on all the medical specialties is done by quotas which are set according to the needs of the country in doctors practicing in medical specialties. The internship periods (of 6 months each) and their distribution between specialties, in order to validate a given specialty, are specified in advance by the college of each specialty. Every six months, all trainee residents in the country (more than 2,000) gather over ten days at the Faculty of Medicine of Tunis, the Tunisian capital, to choose the next 6-month rotation. Within the chosen specialty, the candidate chooses according to seniority first (300-600 in each residency level), and then classification in the corresponding level afterwards.

Protocol: The study protocol was approved by the local Institutional Review Board of Fatouma Bourguiba Teaching Hospital, Monastir (reference #2013/108). All the medical residents gathered at the faculty of medicine of Tunis, between December 14 and December 22, 2015 for the choice of the next 6 month-rotation, and were invited to answer an anonymous, self-administered questionnaire, immediately after having made their choice. The questionnaire covers their civil and marital status, the specialty chosen, their level of advancement in the specialty (duration 4 years for medical specialties and 5 years for surgical specialties), and items of the Hospital Anxiety and Depression score (HAD) questionnaire[22].

Measurements : The questionnaire explored three fields: socio-demographic data, work-related characteristics, and HAD score.

Socio-demographic information concerned the gender, age, marital status, number of dependent children if married or divorced.

Work-related characteristics included specialty, the level achieved so far in the specific curriculum of each specialty, the number of shifts per month, whether the shift was followed by a day of safety rest, and total working hours per week. For the statistical analysis purpose, specialties were split into four groups according to the associated workload: medical (example dermatology, pulmonology, rheumatology, psychiatry, fundamental specialties such as histology, physiology etc…) ; medical and surgical (example: ophthalmology, gynecology-obstetrics, otorhinolaryngology etc…); medical specialties with high workload (example: critical care medicine, emergency medicine, cardiology), and surgical specialties with high workload (neurosurgery, cardiovascular surgery etc).

The survey tool used in our study was Hospital Anxiety and Depression score (HAD) scale that was developed by Zigmond & Snaith [22]**.** It is a brief questionnaire (containing 14 items), and was originally designed to detect emotional disturbances in non-psychiatric patients treated at hospital clinics. It is a self-report rating scale designed to measure both anxiety and depression. It consists of two subscales, each containing seven items on a 4-point Likert scale (ranging from 0-3). Participants were told that the questions asked related to their mental state during the last two weeks. HAD is scored by summing the ratings for the 14 items to yield a total score, and by summing the ratings for the 7 items of each subscale to yield separate scores for anxiety and depression. Two cutoff scores are validated for detecting anxiety and depression, namely 11 for participants who screen positive for anxiety/depression and 8 for probable anxiety/depression.

The survey was written in French and self-completed by each resident who has agreed to participate in the study. The language of the survey is not actually a barrier to the residents' completion of the survey, because that is the language of all medical studies in the country. The total for depression, anxiety subscales the whole HAD scale were calculated by a resident from our unit**.**

Statistical analysis :

The study design focused on determination of the number of residents who met the criteria for anxiety and depression. Continuous variables were expressed either as means ± Standard

Deviations or medians and inter-Quartile Ranges (IQR), according to normal or skewed data distribution. The dichotomous variables were expressed as numbers and percentages. Adjusted Odds Ratios (ORs) and 95% Confidence Intervals (CIs) for each variable were calculated.

Prevalence of anxiety and depression were calculated and correlated to socio-demographic and work-related characteristics. Chi-square tests were carried out to compare the prevalence of anxiety and depression between groups. We used multivariable Poisson regression to identify explanatory variables with a statistically significant effect on the total HAD score.

Statistical significance was denoted by ***p***-values less than 0.05. All statistical procedures were performed using IBM SPSS Statistics 21.0 software.

Participants and Public involvement: No participants were involved in setting the research question or in the design or conduct of the study. No participants were asked to advise on interpretation or writing up of results. There are no plans to disseminate the results of the research individually to study participants.

Results:

During the study-period corresponding to December 14th to December 22nd 2015, 1700 out of 2200 (77%) medical residents from all levels and different specialties answered the survey. They had a mean (±SD) age of 28.5±2 years with a predominance of the female gender (60.8%); 38.5% were married, of whom 19% had at least one child (Table I).

Residents declared they worked for a mean of 62±21 hours per week; 73% (1239) among them worked night shifts with a mean number of 5.4±3 per month, of whom only 8% (98) declared that the shift was systematically followed by a day of safety rest (Table I).

The median HAD score amounted to 19 [IQR: 14 ; 23], split on the anxiety subscale (HAD-A) : 10 [IQR: 7 ; 12], and the depression subscale (HAD-B): 9 [IQR: 6 ; 11].

Overall, 742 (43.6%) residents reached the cut-off defining definite anxiety state (ie a score ≥11), and 519 (30.5%) reached the scale level defining definite depression. Out of these residents, 342 (20%) had both anxiety and depression. In the remaining, the prevalence of probable anxiety score (ie a score ≥8) was 30.5%, and that of probable depression was 31.5%. Tables II and III depict the association between demographic and workload characteristics, and the occurrence of anxiety or depression, respectively.

In univariate analysis, comparison of the group of residents with definite anxiety (HAD-A ≥ 11) to those without definite anxiety (HAD-A < 11), disclosed the following variables as significantly associated with the prevalence of anxiety: higher age, married status (42% vs. 36.7%, p=0.027), and female gender (66.7% vs. 56.2%, p<0.0001) The fifth level of residency course (13.9% vs. 9.7%, p=0.009), and the choice of medical/surgical specialties (15.9% vs. 10.8%, p=0.018) were also significantly associated with anxiety. Medical specialties (45% vs. 54.2%, p <0.0001) were on the contrary associated with a lower risk of developing anxiety symptoms (Table II).

In comparison to residents without definite depression (HAD-D < 11), the group of residents with definite depression (HAD-D ≥ 11) were older, and more often married (45.7% vs. 36.2%, p<0.0001). Moreover, surgical specialties associated with high-workload (22.9% vs. 17.5%, p=0.011) were significantly associated with depressive symptoms in contrast to medical specialties (44.7 vs. 52.6%, p=0.003) which were associated with lower depressive symptoms (Table III). The number of shifts per month, and working hours per month were associated with both anxiety and depressive cases (Table II and III).

The Poisson regression analysis disclosed the following variables as associated with total HAD score: age (OR = 1.014, 95% CI, 1.006-1.023, p = 0.001); female gender (OR = 1.114, 95% CI, 1.083-1.145, p <0.0001); night shift number per month (OR = 1.048, 95% CI, 1.016-1.082, p = 0.03), working hours per week (OR = 1.008, 95% CI, 1.005-1.011, p = <0.0001) . Compared with medical specialties, medico-surgical ones were independently associated with a higher HAD score (OR = 1.459, 95% CI, 1.172-1.816, p = 0.001; fig 1).

Discussion

This large survey encompassing 1700 out of the 2200 Tunisian medical residents brought together for the periodic process of choosing internship positions in their specialties, shows that 43.6% of them had definite criteria of anxiety, and 30.5% had depression. The diagnosis of anxiety or depression was probable in an additional 30% each. Higher scores of anxiety-depression were significantly associated with older age, female sex, and the heavy burden of work imposed on a weekly or monthly basis as reflected by the high number of weekly working hours, the number of night shifts per month, and the choice of a specialty with higher workload (surgical or medical-surgical specialty compared to medical specialty). Of interest, this survey unveils a very demanding health system imposed on Tunisian medical residents as reflected by the average working hours per week (60 hours), and the number of night shifts per month (6 on average regardless of the type of specialty), most often without a day of safety rest.

Although, mood disorders and physician distress are more prevalent among medical professionals compared to the general population, information is lacking about their prevalence in Tunisia [5 23 24]. This first survey on the subject in our country, enrolled 77% of potentially concerned medical residents, yielding a snapshot of the burden incurred by residents from all specialties in their everyday practice. The use of the French version of the HAD questionnaire should not be considered as a barrier to the residents' completion of the survey, because that is the language of all medical studies in the country.

International studies stressed the fact that medical residents usually have higher rates of depression than the general population[15 25]. Estimates of the prevalence of depression or depressive symptoms among resident physicians vary from 3% to 60% with a median of 28.8% according to a recent meta-analysis of 54 studies[15]. This proportion is lower than that recorded in our study whether we consider the rate of definite or probable depression (62%), or even when we only consider the cases qualifying for definite depression (30.5%). Of interest, this meta-analysis emphasized the difference in the methodological approach to address the issue of depression in medical residents (cross sectional studies to assess the prevalence vs longitudinal studies which inform on the incidence)[15]. The meta-analysis highlighted also the great variability in the instruments used (no less than 13 different instruments were used in the 54 studies)[15]. A prospective cohort

study conducted in Switzerland and using the HAD inventory used in our study disclosed a prevalence of anxiety in 30% of the second year residents, and 20% of the fourth and sixth year residents; depressive symptoms were present in 15% and 10%, respectively[26]. However, benchmarking with countries with socio-economic similarities could be more insightful. In a study including 118 residents from the American University of Beirut, 22% qualified for moderate to major depressive symptoms while only 8% had anxiety[27]. Moreover, in a cross sectional study conducted among residents of various specialties in Saudi Arabia, the prevalence of moderate to severe depressive symptoms was around 20% [17].

Resident physicians share the same known causes of depression than the general population: physical health, lifestyle, marital status, history of previous depression, childhood issues, religiosity etc[1 4]. They have in addition specific factors according to the way the work is done, its everyday planning, and the constraints inherent to their career development [4]. These risk-factors correspond to the difficulty of their specialty, postgraduate year, stress at work, current rotation difficulty, working hours, shift number etc…[4 15 28]. In our study the Poisson regression model disclosed the following items as statistically associated with the occurrence of anxiety-depression: age, female sex, practice of a specialty generally accepted as very demanding and difficult, and the heavy burden of work imposed on a weekly or monthly basis as reflected by the weekly working hours, and the night-shift number per month. Most of these risk-factors have been reported elsewhere, or are intuitive, but it is their magnitude that makes this study important.

The occurrence of depression should be considered as a major event in the young physician's career or even life. It has been shown that once present, depression as well as burnout (another consequence of work-related chronic stress) may persist throughout the whole residency duration, or even beyond [29 30]. In a nationwide survey involving 3500 Canadian physicians, Sullivan et al reported that 55% found that medicine as a profession impacted negatively on their family and personal life, while 65% reported that opportunities to change career despite dissatisfaction were limited [31]. Depression is also a source of decreased concentration at work, an increase in the rate of medical errors, work dissatisfaction and conflicts, impaired sleep quality, and a greater propensity to attrition, and even suicide ideation [9 32 33].

Considering the high prevalence of anxiety and depression among Tunisian medical residents, every effort aiming at improving the mental health of young physicians should be encouraged. Any strategy should target both the individual level to amend the identified and potentially actionable risk-factors, and include more measures targeting the general organization of residents' work modalities, and their relationship with the hierarchy and administration.

The resident physician should first become aware of the mental health issue and seek help in particular those with a previous personal history of depression[34]. We did not investigate whether the participating residents sought for, or actually had psychological counseling, but we strongly believe that most did not. Structures able to provide aid to health professionals exposed to, and suffering from stress, anxiety, depression, are anyway non-existent in Tunisian hospitals. Our study suggests that such structures can no longer be considered an option, but the Ministry of Health should provide support at institutional level. At individual level, more generally accepted risk factors such as older age, gender, marital status, stressors outside of work, sleep deprivation, or lifestyle, require more personal attention and lifestyle education[4]. The current study was not designed to allow participants' identification so that they could be given individual information and act on it. Future studies targeting preferentially residents (or specialties) at high risk of anxiety, depression, or burnout, should consider such feedback for more specific training programs.

Residency program factors and the pace of work should also be better managed. While these details were totally non-existent in Tunisia, this has been recently fixed through a law issued on March 9, 2018 whose purpose is the definition of the status of Tunisian interns and residents[35]. This law, which has been torn out following long negotiations, and a strike that lasted more than 6 weeks, defines for the first time the role and duty of residents. The maximum number of weekly working hours and that of night shift frequency have been clearly defined and have been reduced to a maximum of 40 hours and two night shifts per week, respectively. A day of safety rest following every night shift has been rendered mandatory. Although still debated, the issue of work-hour restriction could be effective in reducing high emotional exhaustion, despite the fact that it carries the risk of alteration in the quality of care and education by reducing the number, and actual presence of medical residents [36].

***Legend Figure1*:** Risk Factors associated with Total HAD Score

Authors' contributions

Study Concept and design: MM and FA; Data Acquisition: MM; Analysis and interpretation of the data: MM, LOB, ZH, IO, FD, FA; All authors read and approved the final manuscript. MM and FA had full access to the data and take responsibility for its integrity and the accuracy of the analyses.

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Data Sharing statement: dataset is available by contacting FA at f.abroug@rns.tn

Table I : Demographic and work characteristics of the study population (n=1700) :

Sex ratio (M/F)		667/1033
Age, med [IQR]		28 [27 ; 30]
Marital Status	**Single**, n(%)	1036 (61)
	Married, n(%)	655 (38.5)
	Divorced, n(%)	9 (0.5)
Number of Children	**Zero**, n(%)	343 (20.2)
	One, n(%)	235 (13.8)
	More than one, n(%)	86 (5.1)
Residency Level (year)	**I,** n(%)	320 (18.8)
	II, n(%)	410 (24.1)
	III, n(%)	434 (25.5)
	IV, n(%)	340 (20)
	V, n(%)	196 (11.5)
Specialty*	**Medical,** n(%)	854 (50.2)
	Medical and Surgical, n(%)	221 (13%)
	High-workload Medical specialties, n(%)	299 (17.6)
	High-workload Surgical specialties, n(%)	326 (19.2)
Working hours per week, med [IQR]		60 [48 ; 76]
Night shifts per month, med [IQR]		6 [4 ; 7]
Recovery day following night shift, n (%)		98 (8)

**Specialties were split into four categories according to everyday difficulties: medical (example dermatology, pulmonology, rheumatology, neurology, psychiatry, fundamental specialties like histology, physiology etc) ; medical and surgical (example: ophthalmology, gynecology-obstetrics, otorhinolaryngology etc); high-workload medical (example: critical care medicine, anesthesiology, emergency medicine, cardiolgy), and high-workload surgical specialties (surgery, pediatric surgery, orthopedics, neurosurgery, urology, cardiovascular surgery etc).*

Table II : *Demographic and workload characteristics and their association with anxiety :*

		No Anxiety	Definite Anxiety	*p*
n (%)		958 (56.4)	742 (43.6)	
Age, *mean±SD*		28.5±1.9	28.7±2	**0.008**
Gender				**0.0001**
	Male	420 (43.8)	247 (33.3)	
	Female	538 (56.2)	495 (66.7)	
Marital Status				**0.027**
	Single	606 (63.3)	430 (58)	
	Married	352 (36.7)	312 (42)	
Level of Residency				**0.005**
	I	188 (19.6)	132 (17.8)	
	II	244 (25.5)	166 (22.4)	
	III	251 (26.2)	183 (24.7)	
	IV	182 (19)	158 (21.3)	
	V	93 (9.7)	103 (13.9)	
Specialty				**0.018**
	Medical	519 (54.2)	334 (45)	
	Medical and Surgical	103 (10.8)	118 (15.9)	
	High-workload Surgical specialties	181 (18.9)	145 (19.5)	
	High-workload Medical specialties	155 (16.2)	145 (19.5)	
Shifts/month, *mean±SD*		4.9±3	6±2.9	**0.0001**
Working Hours/week, *mean±SD*		58.8±20	66.4±20	**0.0001**

Table III : *Demographic and workload characteristics and association with depression cases*

		No depression	Definite depression	*p*
N (%)		1181 (69.5)	519 (30.5)	
Age, *mean±SD*		28.3±1.8]	29±2	**0.007**
Gender				0.11
	Male	453 (38.4)	214 (41.2)	
	Female	728 (61.6)	305 (58.8)	
Marital Status				**0.0001**
	Single	754 (63.8)	282 (54.3)	
	Married	427 (36.2)	237 (45.7)	
Level of Residency				**0.0001**
	I	263 (22.3)	57 (11)	
	II	292 (24.7)	118 (22.7)	
	III	294 (24.9)	140 (27)	
	IV	218 (18.5)	122 (23.5)	
	V	114 (9.7)	82 (15.8)	
Specialty				**0.006**
	Medical	621 (52.6)	232 (44.7)	
	Medical and Surgical	156 (13.2)	65 (12.5)	
	High-workload Surgical specialties	207 (17.5)	119 (22.9)	
	High-workload Medical specialties	197 (16.7)	103 (19.8)	
Shifts/month, *mean±SD]*		5±3	6±2.9	**0.0001**
Working Hours/week, *med [IQR]*		60±20	66±20	**0.0001**

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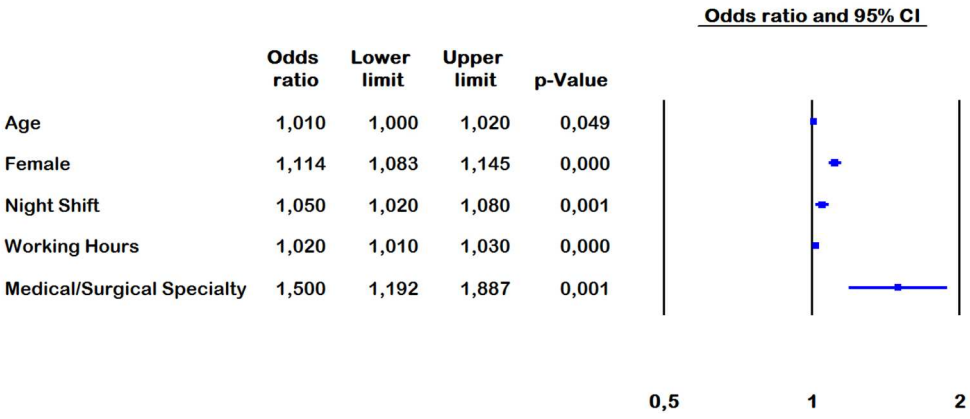

Figure1: Risk factors

114x52mm (300 x 300 DPI)

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation	
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	X
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	X
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	P2
Objectives	3	State specific objectives, including any prespecified hypotheses	P2
Methods			
Study design	4	Present key elements of study design early in the paper	P5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	P5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	P5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	P6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	P6
Bias	9	Describe any efforts to address potential sources of bias	P6
Study size	10	Explain how the study size was arrived at	P7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	P7
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	P7
		(*b*) Describe any methods used to examine subgroups and interactions	NA
		(*c*) Explain how missing data were addressed	P7
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	NA
		(*e*) Describe any sensitivity analyses	P7
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	P8
		(b) Give reasons for non-participation at each stage	P8
		(c) Consider use of a flow diagram	NA
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	TableI
		(b) Indicate number of participants with missing data for each variable of interest	NA
Outcome data	15*	Report numbers of outcome events or summary measures	P8
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	P8

		(*b*) Report category boundaries when continuous variables were categorized	P8
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	NA
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	P9
Discussion			
Key results	18	Summarise key results with reference to study objectives	P10
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	P10
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	P10-11
Generalisability	21	Discuss the generalisability (external validity) of the study results	P11
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	P1

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.