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Trend in Hospital Admissions of Drug Addicts and Associated Factors from 2006 to 2015: an Observational Study on the Hospitals' Discharge Registries from a Region of Central Italy

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Key words: Addiction, hospital admission, Administrative data, Italy, Risk factors, Abuse
Parole chiave: Dipendenza, ospedalizzazioni, Dati amministrativi, Italia, Fattori di rischio, Abuso

Abstract

Background. *Several social, economic and political factors have contributed to the global spread of alcohol and other drugs. Drug addiction represents a huge expense for the society in terms of direct and indirect health and social consequences, as it is associated with numerous medical issues such as HIV, other infec**tions and psychiatric disturbances.***

Objectives. *The aim of this study was the assessment of the hospital admissions among drug addicted patients in Abruzzo Region, central Italy, from 2006 to 2015, in order to clarify the specific causes of hospitalization.*

Methods. *Data were collected from all hospital discharge records, taking into account only the hospital discharge registrations coded 304 (drug dependence). Multivariate logistic regression was performed to evaluate factors associated with main causes of the admission.*

Results. *Between 2006 and 2015, an amount of 2,159 drug-addicted subjects, aged 38.0±9.7 years, were admitted to hospital. Most of the admissions occurred in public hospitals (2,039, 94.4%), through the emergency room access (1,503, 69.6%) From an amount of 2,159 hospitalizations, 1,178 (54.6%) were first and 981 (45.4%) were subsequent admissions. The most frequent cause of hospitalization was "Psychosis" (419, 19.4%). The trend by range of age showed a progressive reduction in hospital admissions for patients aged < 45 y. Further, an increase in the hospitalization rate was estimated over recent years among drug addict subjects aged 25-45 years. Cannabis consumption was associated with mental disorder admissions (OR: 3.16, p<0.001), opioid consumption was associated with hepatic disorder admission (OR:2.16, p<0.001) and cardiovascular admissions (OR: 1,78, p<0.001), and cocaine was associated with cardiovascular admissions (OR:1,55, p:<0.001).*

Conclusions. *Mental disorders result to be the leading cause of hospitalization among drug-addicts, principally associated with cannabis abuse. Opioid and cocaine abuse was associated with hepatic and cardiovascular disorders.*

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Abbreviations: HDR= hospital discharge registry; DRG= Diagnosis Related Group; MDC= Major Diagnostic Category; SD= Standard Deviation; IQR= Interquartile Range; HCV= Hepatitis C Virus; HBV= Hepatitis B Virus; HIV= Human Immununodeficency Virus

Introduction

Numerous social, economic and political factors have contributed to the global spread of alcohol and other drugs, creating enormous costs for the society in terms of direct and indirect. involvement. During the last ten years, drug abuse prevalence changed across Europe, with an increasing trend for cocaine and synthetic drugs consumption (1). Despite this, cannabis remains the leading abused drug. Italy, that is the third European country for drug consumption, during the last 20 years has invested in establishing monitoring capacity, with the aim to better understand the drug-addiction situation (3). Drug abuse is associated with numerous medical consequences, such as HIV, psychiatric disturbances, neurologic complications, cardiovascular problems and infections. Drug use may also cause indirect health consequences due to typical drug-addiction behaviors (e.g., needle sharing, unprotected sex) leading to serious medical complications (2). Data on drug-related hospital admissions can be useful for the identification of such health-related disorders that are not demonstrable by using other information sources. In highly developed countries, it is estimated that 5% of hospital admissions are related to illegal substances use (3). Admissions mainly concern internal medicine departments, cardiology and pulmonary medicine, and refer principally to blood system and respiratory disorders (4). A recent study showed that a significant part of emergency department accesses, involve agitated patients (5). In particular, the drugs most commonly reported in the presentations with psychosis were cannabis and amphetamine (6). In Italy, drug-related admissions amounted to 6,083 in 2016, showing a hospitalization rate of about 10 admissions every 100,000 residents. Moreover, most of them concerned subjects belonging to the age group between 25 and 44 years (7).

The present study aimed to assess all hospital admissions of drug addicted patients performed in Abruzzo, an Italian region, from 2006 to 2015, and to evaluate the associated causes of hospitalization.

Materials and methods

The study considered all hospital admissions performed between January 1, 2006 and December 31, 2015 in Abruzzo, a region in the center of Italy. Abruzzo region counts over 1.2 million inhabitants and has 29 hospitals (18 public hospitals and 11 private clinics). Data were collected from all Hospital Discharge Records (HDRs), using the hospital information system. This system includes information about the patients' demographic characteristics, a Diagnosis Related Group code (DRG, grouped in 25 Major Diagnostic Category - MDC) used to classify the admissions and up to 6 diagnoses and 6 procedures performed during the hospitalization. For the study, only admissions with code 304 (drug dependence) were taken into account, and only when registered as the principal diagnosis or as one of five secondary diagnoses. The following socio-demographic variables were also collected: age, citizenship, marital status, scholarship, hospitalization length, admission procedure and discharge procedure.

Statistical analysis

Quantitative variables were summarized as mean and standard deviation (SD) or as median and interquartile range (IQR), according to their distribution. Qualitative variables were summarized as frequency and percentage. Annual standardized hospitalization ratios were computed, as well as the annual trends. The standardization was performed taking into account the annual population of Abruzzo region during the study period. When appropriate, non parametric

trend analysis or ANOVA for repeated measures were performed to evaluate annual trend for hospital admissions, age at the admission and length of stay. Multivariate logistic regression with backward selection was performed to evaluate factors associated with the cause of admission. For these analyses age less than 25 years of age, gender, marital status, type of drug abused, HCV, HBV and HIV infections where considered as covariates. Only covariates with p-value less than 0.10 were maintained in the model. P-value less than 0.05 was considered statistically significant. The statistical analysis was performed using IBM Spss Statistics v20.0 software (SPSS Inc. Chicago, Illinois, USA).

Results

Between 2006 and 2015, an amount of 2,159 drug-addict patients (38.0±9.7 years of age) was admitted to a hospital in Abruzzo. Among them, 1,733 subjects were male (80.3%), and 870 (40.3%) were unmarried. The most frequently used drugs were opioids. All patients' characteristics are reported in Table 1. Most of the subjects were admitted through the emergency room (1,503, 69.6%), and hospitalized in public hospitals (2,039, 94.4%). The average length of hospital stay was 7 days (IQR 3-13), then 1,598 (74.0%) patients were discharged at home and 366 (17%) were voluntarily dismissed (Table 2). From an amount of 2,159 hospitalizations, 1,178 (54.6%) were categorized as first admissions, and 981 (45.4%) as subsequent hospitalizations. During the study period, more than 411 patients (19.0%) performed at least one repeated admission, and one patient was even admitted 22 times. Overall, the most frequent DRG in the discharge registry was "Psychosis" (419, 19.4%), followed by "Alcohol/Drug Abuse or Dependence without Rehabilitation Therapy without comorbidity or complication" (246, 11.4%) and "Alcohol/Drug Abuse or Dependence, Left against Medical Advice" (161, 7.5%), as shown in Table 3. The most frequently represented MDCs were psychiatric disorders (558, 25.8%),

Table 1 - Patients' Characteristics

Age *mean±SD*	38.0 ± 9.7
Gender (*n and %)*	
Male	1,733 (80.3)
Female	426 (19.7)
Nationality	
Italian	2,080 (96.3)
Other	79 (3.7)
Marital Status (*n and %)*	
Unmarried	870 (40.3)
Married	383 (17.7)
Separed/Divorced	89 (4.2)
Other/Unknown	817 (37.8)
Instruction (*n and %)*	
Graduated	56 (2.6)
High School	231 (10.7)
Middle School	251 (11.6)
Elementary School/Nothing	225 (10.4)
Unknown	1,396 (64.7)
Type of Dependence (*n and %)*	
Opioid	829 (38.4)
Cocaine	117 (5.5)
Cannabinoid	63 (2.9)
Combination	140 (6.5)

Table 2 - Hospital admission characteristics

Duration in Days (*median and IQR)*	7 (3-13)
Type of Admission (*n and %)*	
Emergency Room	1,503 (69.6)
Ordinary	557 (25.8)
Other	99 (4.6)
Type of Discharge (*n and %)*	
Ordinary at Home	1,598 (74.0)
Voluntary Discharge	366 (17.0)
Domiciliary Hospitalization	71 (3.3)
Death	30 (1.4)
Other	94 (4.3)
Repeated Admissions *n(%)*	981 (45.4)

Table 3 - Diagnosis Related Groups Distribution

Code	DRG	N (%)
430	Psychosis	419 (19.4)
523	Alcohol/Drug Abuse or Dependence without Rehabilitation Therapy Without Comorbidity or Complication	246 (11.4)
433	Alcohol/Drug Abuse or Dependence, Left Against Medical Advice	161 (7.5)
205	Disorders of Liver Except Malignancy, Cirrhosis, and Alcoholic Hepatitis with Comorbidity or Complication	154 (7.1)
202	Cirrhosis & Alcoholic Hepatitis	78 (3.6)
428	Disorders Of Personality & Impulse Control	77 (3.6)
490	HIV with or without other Related Condition	71 (3.3)
	Other	953 (37.0)

followed by hepatobiliar disorders (285, 13.2%) and neurological disorders (132, 6.1%), as described in Table 4. Particularly, psychosis (Excitative type psychosis, 221 cases, and Unspecified psychosis, 121 cases), and Chronic Hepatitis C were the most frequent principal diagnoses. Over the study period, the number of admissions per year moved from 222 cases in 2006 to 259 cases in 2015, showing a downturn in the years from 2009 to 2011 as reported in Table 5. In particular the standardized year trend significantly grew from 16.7 cases over 100,000 inhabitants to 19,5 ($p<0.001$). Patients' mean age at the admission presented a progressive reduction from 38.7 to 35.8 years, by contrast the median length of stay remained constant. The trend by range of age showed a progressive reduction in hospital admissions among patients aged over 45 (from 5.87 to 3.01 admissions per 100,000 inhabitants), while there was an increase in admissions of patients between

Table 4 - Distribution of major diagnostic categories and principal diagnoses

MDC n (%)				
Mental Disorders 558 (25.8)	Hepatobiliary System and Pancreas Disorders 285 (13.2)	Nervous System Disorders 132 (6.1)	Respiratory System Disorders 129 (6.0)	Circulatory System Disorders 118 (5.4)
Excitative type psychosis 221 (39.6)	Chronic hepatitis C 122 (42.8)	Encephalitis and myelitis 31 (23.5)	Bacterial pneumonia 39 (30.2)	Phlebitis and thrombophlebitis of deep veins of lower extremities 38 (32.2)
Unspecified psychosis 121 (21.7)	Hepatic encephalopathy 60 (21.1)	Acute suppurative otitis 24 (18.2)	Bronchopneumoia, organism unspecified 28 (21.7)	Acute and subacute bacterial endocarditis 21 (17.8)
Acute paranoid reaction 83 (14.9)	Alcoholic Hepatitis 22 (7.7)	Meningitis due to other organisms 9 (6.8)	Other diseases of lung 10 (7.8)	Cardiac arrest 10 (8.5)
Major depressive affective disorder 48 (8.6)	Chronic hepatitis B 22 (7.7)	Others 68 (51.5)	Unspecified pleural effusion 9 (7.0)	Acute venous embolism and thrombosis of other specified veins 9 (7.6)
Paranoid schizophrenia, acute exacerbation 33 (5.9)	Others 59 (20.7)		Abscess of lung 7 (5.4)	Others 40 (33.9)
Others 52 (9.3)			Others 36 (27.9)	

Table 5 - Trend in Hospital Admissions of Drug Addicts Between 2006 and 2015

	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	p-value
Admissions*	16.72	15.96	16.87	13.70	13.48	13.78	15.14	18.22	19.20	19.50	**<0.001**
Age *mean±SD*	38.7±11.2	39.0±9.8	39.5±9.8	39.3±11.2	39.6±9.2	38.2±9.4	37.2±9.3	36.3±9.2	36.6±9.0	35.8±8.1	0.685
Hospitalization Duration *median(IQR)*	8.0 (3.8-13.0)	7.0 (3.0-14.0)	7.0 (3.0-12.0)	7.0 (3.0-12.0)	7.0 (3.0-12.0)	6.0 (2.0-14.0)	6.0 (2.0-11.0)	6.0 (2.0-12.0)	6.0 (3.0-11.0)	7.0 (3.0-16.0)	0.756

* Standardized hospitalization ratios /100,000 inhabitants

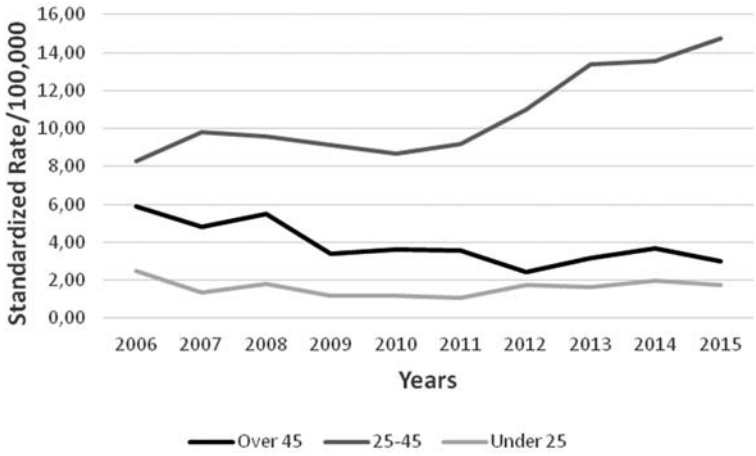

Figure 1 - Trend in Hospitalization by Age (Standardized Ratios /100,000 Residents

25 and 45 years of age (from 8.28 to 14.76 per 100,000 inhabitants), as shown in Figure 1. The multivariate analysis showed that age less than 25 (OR=1.90, 95% CI 1.11-2.98, p=0.010), being unmarried (OR=1.32, 95% CI 1.01-1.74, p=0.032), opioid consumption (OR=0.21, 95%CI 0.16-0.26, p<0.001) and cannabinoid consumption (OR=3.16, 95%CI 1.77-5.69, p<0.001), were associated with admission due to mental disorders. Oppioid dependent patients were likely to be admitted for Hepatobiliary Disorders (OR=2.16, 95%CI 1.32-6.89, p<0.001). Cocaine and opioid abuse were associated with circulatory system disorders admissions (respectively OR 1.55, 95%CI 1.07-2.77, p=0.002 and OR 1.78, 95%CI 1.10-3.98, p<0.001). Multivariate models are shown in Table 6.

Discussion and conclusions

The aim of this study was to describe a 10-year trend in hospital admissions related to drug dependence in Abruzzo, a region of Central Italy. As a result of the study, opioids

Table 6 - Factors associated with hospital admission diseases

	OR	95%CI	p-value	adjOR	95%CI	p-value
Mental Disorders						
Age <25years	2.11	1.19-3.52	0.009	1.90	1.11-2.98	0.010
Marital Status				<0.001		<0.001
Married	Ref			ref		
Unmarried	1.44	1.05-2.01	0.021	1.32	1.01-1.74	0.032
Separated/Divorced	0.69	0.28-2.08	0.685	0.54	0.31-1.66	0.462
Cannabinoid consumption	4.75	2.01-6.98	<0.001	3.16	1.77-5.69	<0.001
Oppioid consumption	0.33	0.19-0.41	<0.001	0.21	0.16-0.26	<0.001
Hepatobiliary System and Pancreas Disorders						
HCV	7.10	3.10-12.25	<0.001	6.80	2.11-10.5	<0.001
HBV	2.22	1.33-4.89	<0.001	1.95	1.21-4.05	<0.001
Oppioid consumption	2.58	1.44-7.29	<0.001	2.16	1.32-6.89	<0.001
Nervous System Disorders						
HIV	1.99	1.24-5.10	<0.001	1.81	1.17-4.87	0.002
Respiratory System Disorders						
Age <25years	0.80	0.65-0.95	0.021	0.88	0.62-0.98	0.041
Circulatory System Disorders						
Age <25years	0.71	0.48-0.89	0.016	0.75	0.56-0.91	0.027
Oppioid consumption	2.18	1.19-4.33	<0.001	1.78	1.10-3.98	<0.001
Cocaine consumption	1.59	1.09-2.76	0.001	1.55	1.07-2.77	0.002

are the most frequently used substances by the subjects admitted to hospital, according to our study. The great part of admissions were performed through the Emergency Departments, confirming the finding of Liu et al. (8). Other characteristics of studied admissions were the high frequency of voluntary discharges and the high number of hospital readmissions during the study period. In fact, as presented by McNail et al. (9) and T Yong et al. (10), a serious problem of most drug addicts was their voluntary discharge against medical advice (17.0% in this sample), which implies, as a consequence, a substantial risk of readmission and mortality. The first cause of admission among drug addicted patients was mental diseases, confirming the evidence reported by Pavarin et al. (7) and Mordal et al. (11). It's well known, in fact, that cannabis use is related to schizophrenia, mania, panic disorder and major depression (8, 12, 13). Also methamphetamine dependence is reported to be associated with primary psychiatric disorders and primary mood disorders (13). These results, associated with the short length of stay of these patients, focused the attention on the managing of the psychiatric disease in the out-of-hospital environment, together with an adequate psychiatric and addiction therapy (14). Other relevant causes of admission were related to the addiction itself, as reported in Table 3. Most of the admission diagnoses were related to liver disease: hepatitis was more common among intravenous drug users (14) due to the sharing of contaminated needles. However, over the past decade, type and features of drug abuse have changed. Previously, substances use was considered a problem confined to urban ghettos, where intravenously administered heroin was the most common drug abused.

To date, smoking marihuana and hashish, sniffing and smoking heroin, and ingesting LSD, amphetamines, barbiturates, other tranquilizers, and psychotomimetic drugs are the most common modes of drug consumption (15). Apart from heroin, each type of drug plays a role in hepatic damage. Cannabis abuse does not cause acute hepatotoxicity, although it is demonstrated that daily cannabis smoking is a risk factor for liver fibrosis progression (16, 17). Amphetamine-induced hepatotoxicity can show itself, up to four weeks after ingestion, as mixed hepatitis (18). Moreover, amphetamines, when used to bear exhaustive dancing at hot night 'raves', triggers the heat stroke-like syndrome causing hyperthermia, shock, ischemia, and hepatic necrosis in the drugged dancers (19). Cocaine is currently the most popular drug in North America and Europe. It leads to a range of liver abnormalities ranging from mild asymptomatic elevation in liver enzymes to severe liver injury. A study carried out in the United States identified 39 patients presenting acute cocaine intoxication and rhabdomyolysis. Evidence of hepatic dysfunction was observed in 23 patients (20). Trend analyses highlighted a significant increase in hospital admissions of drug-addicted subjects, mainly in the years ranging from 2011 to 2015. These analyses focused the attention on the progressive reduction in the age of drug-addicts at their admission to hospital: in fact, the trend showed an upturn in the age range between 25 and 45 years, as evidenced by the findings of Giordano et al. (21). Multivariate analyses performed to evaluate factors associated with the cause of the hospitalization confirmed the previously discussed findings. In fact, opioid abuse was associated with Hepatobiliary System Disorders, due to the intravenous consumption of these drugs that lead to HCV/HBV or other infection. Cannabis consumption was confirmed as factor associated with Mental Disorders, as previously anticipated. In particular, high doses of novel synthetic cannabinoid drugs can lead to acute psychotic symptoms (22-23). About cardiovascular disease, as confirmed by this study, cocaine is a well-known cardiotoxic agent. In particular, there is an established connection between cocaine use and myocardial infarction, arrhythmia, heart failure, and sudden cardiac death. Numerous mechanisms have been hypothesized to explain the contribution of cocaine to these conditions. Among these, cocaine may lead to infarction by causing coronary artery vasoconstriction and accelerated atherosclerosis, and by initiating thrombus formation (24). In addition, opioid abuse resulted in significant association with cardiovascular diseases: despite limited data available, it seems that chronic opioid administration may be associated with an increased risk for cardiac-related adverse effects, as reported by Chen et al. (25). In conclusion, the hospital admission rate of drug addicted patients has increased over recent years, specifically among patients aged 25-45. Mental disorders are the leading cause of hospitalization among drug-addicts, who are likely to incur in frequent readmissions and to apply for voluntary discharge. Drug abuse is a public health problem that shifts the attention on managing the psychiatric disease in the out-of-hospital environment, highlighting the need for an adequate psychiatric and addiction therapy. In addition, the knowledge of diseases associated with drug abuse can led to the improvement of preventive strategy in managing drug addiction and its consequences.

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Limitations: The results of this study should be considered in the light of the following limitations: first,

the identification of diagnosis was based on ICD-9-CM codes that did not take into account the severity of conditions. Second, the use of administrative data might be limited by the reliability of certain types of information, such as drugs therapy and clinical information. Third, the drug dependence code (304) could be not reported, due to the lack of the information or to a miscoding (26).

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Ethical approval: The study was conducted in conformity with the regulations on data management of the Regional Health Authority of Abruzzo and with the Italian Law on privacy (Art. 20-21 DL 196/2003) published on the Official Journal n. 190 of August 14, 2004. Data were encrypted prior to the analysis at the regional statistical office, where each patient was assigned a unique identifier. This identifier eliminated the possibility to trace the patient's identity. Administrative data do not need a specific written informed consent.

Riassunto

Andamento temporale delle ospedalizzazioni correlate alla tossicodipendenza e fattori associati dal 2006 al 2015: studio osservazionale sulle schede di dimissione ospedaliera di una regione del Centro Italia

Premessa. Diversi fattori sociali, economici e politici hanno contribuito alla diffusione globale di alcol e altre droghe. La tossicodipendenza rappresenta una grande spesa per la società in termini di conseguenze dirette e indirette, in quanto è associata a numerosi problemi medici come l'HIV, diverse infezioni e disturbi psichiatrici.

Obiettivi. Lo scopo di questo studio è stato di esaminare l'epidemiologia dei ricoveri ospedalieri dei pazienti tossicodipendenti in Abruzzo, Italia centrale, dal 2006 al 2015, al fine di valutare le specifiche cause di ospedalizzazione ed i fattori ad esse associati.

Metodi. I dati sono stati raccolti da tutti i registri di dimissioni ospedaliere, prendendo in considerazione solo le ospedalizzazioni riportanti il codice ICD9 legato alla tossicodipendenza (304; tossicodipendenza). Modelli multivariati di regressione logistica sono stati sviluppati per valutare i più importanti fattori associati alle principali cause di ricovero.

Risultati. Tra il 2006 e il 2015, sono stati ricoverati 2.159 soggetti tossicodipendenti, con età media di 38,0±9,7 anni. La maggior parte delle ammissioni è avvenuta in ospedali pubblici (2.039, 94,4%) ed attraverso l'accesso al pronto soccorso (1.503, 69,6%) Da un totale di 2.159 casi, 1.178 (54,6%) sono risultati primi ricoveri e 981 (45,4%) sono stati ricoveri successivi al primo. La causa più frequente di oIumo di cannabis è risultato associato a ricoveri per disturbi mentali (OR: 3.16, p<0,001), l'uso di oppioidi è risultato associato a ricoveri per disturbi epatobiliari (OR: 2.16, p<0,001) e cardiocircolatori (OR: 1,78, p<0,001), e la cocaina è risultata associata a ricoveri per patologie cardiocircolatorie (OR:1,55, p<0,001).

Conclusioni. I disordini mentali risultano essere la principale causa di ospedalizzazione tra tossicodipendenti, principalmente legati al consumo di cannabis. Il consumo di oppioidi e cocaina è principalmente associato a patologie epatobiliari e cardiovascolari.

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