

Etiological Approach of Cholelithiasis in the Beni Mellal-Khénifra Area in Morocco

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Abstract: ***Aims:** The prevalence of cholelithiasis is unknown in the Beni Mellal-Khénifra area in Morocco. This research work aims to achieve an approach to the multiple factors influencing the presence of cholelithiasis in the Beni Mellal-Khénifra area. **Sampling and Methods:** The present study has been carried out during the year 2018 on 226 patients at the Beni Mellal Regional Hospital in Morocco. Observations by polarizing light optical microscopy have been performed on gallstones in order to have selective samples for the constitutional analysis. After having been dried during 24 hours at room temperature these gallstones underwent morphological analysis. A Classification by the Principal Component Analysis (PCA) method has been applied to individuals that are gallstones samples and 8 variables that are: "age"; "gender"; "water quality"; "daily water intake"; "Socio-economic background" and "personal and family history"; "gallstone type"; "cholecystitis type". **Results:** During a four months study, 226 gallstones have been collected from 226 patients of the Beni Mellal regional hospital in Morocco. From each patient we have chosen one gallstone that relatively represents the eventual other gallstone from his gallbladder. The analysis of the results showed a clear female predominance, 198 women of the total collected gallstones with a 87.6% frequency, compared to the case of men (12.4% frequency). Such a result corresponds to 7 as a (woman/man) gender ratio. From the obtained results by the Principal Component Analysis method, we note that there are correlations, positive or negative, between some factors that may influence the presence of the cholelithiasis. **Conclusions:** The present work confirms that cholelithiasis in the Moroccan Beni Mellal-Khénifra area is also predominantly female. In addition, the study confirms that cholelithiasis is multifactorial since diverse factors may influence the presence of this disease.*

Keywords: gallstone, Cholecystitis, Principal Component Analysis

1. Introduction

According to the literature, cholecystitis would affect 10 to 15% of the adult populations in Europe. Controversial aspects of its management have recently been the subject of recommendations for clinical practice [1].

Gallstones can cause changes in the main bile duct or disc, impeding the flow of bile in about 15% of carriers. According to previous researches the lithiasis of the main bile duct would be the major cause [2] - [3]. Through these last years the management of the lithiasis of the main bile duct has been changed. Twenty years ago, a two-step approach was advocated, consisting of a laparoscopic cholecystectomy followed by endoscopy with retrograde cholangiopancreatography for calculus extraction. Currently, some teams have ultrasound endoscopy with sphincterotomy when suspected cholelithiasis is suspected, while other teams undergo treatment within one surgical time. Recent analysis of the literature [4]- [5] shows that an all-surgical strategy does not result in more morbidity-mortality than the two-step strategy; it also prevents the patient from two general anesthesia and two hospitalizations, with a lower cost [4]- [6]. Obesity, a major public health problem [7]- [8] - [9], is a risk factor for cholesterol cholelithiasis, there is indeed a correlation between the body mass index and the frequency of symptomatic or non-symptomatic vesicular lithiasis [7]. In addition, rapid weight loss is also a risk factor for

cholelithiasis by mobilization of endogenous cholesterol whose biliary concentration increases [7] - [10].

This work aims to carry out an approach to the multiple factors influencing the presence of cholelithiasis in the Moroccan Beni Mellal-Khénifra area.

2. Sampling and methods

Our retrospective and descriptive study involved 226 patients (198 women and 28 men) presenting cholelithiasis in the Beni Mellal Regional Hospital in Morocco during the year 2018. An identification form containing information about the patient has been filled. A Classification by Principal Component Analysis (PCA) method was applied to the individuals who are the 226 patients and the 8 variables that are: "age"; "gender"; "water quality"; "daily water intake"; "socio-economic background" and "personal and family history"; "gallstone type"; "cholecystitis type".

We have determined the following characteristics:

- Sociodemographic characteristics
- History
- Biological parameters

A study using polarizing light optical microscopy has been performed on the gallbladders, in order to have selective samples for the constitutional analysis.

3. Results and Discussions

3.1 Patient distribution by gender and age

Among the risk factors influencing cholelithiasis there are the gender and the patients age. In the present work there was a female predominance, 198 women (87.6%) and only 28 men (12.4%). The (woman/man) gender ratio has been 7. The predominance of women in cholelithiasis is evident in this work. This result is consistent with the results of other epidemiological studies whose authors have confirmed that women would be two to three times more affected than men [11]- [12] - [13].

Gallstones are rarely observed before the 10 years age, and less than 5% of cholecystectomies are performed before the 20 years age [11]- [13], because it is rather a pathology of the adult where one has proven that when 800 adults have cholelithiasis, there will be only one child or adolescent [11].

In the present work, the studied population consists of 226 patients who are moderately 45 years old and present cholelithiasis. Such a result is similar to other results that have been cited in research publications[11] - [14].

The patients age that is ranged between 9 and 95 years with a prevalence of 40 to 59 years age (43%), followed by 60 years age (32%). The age below 40 years presents a 25% frequency (Figure 1). We show that the prevalence of cholelithiasis increases with age until a peak between 40 and 69 years and then the prevalence decreases. This result is closer to the results of other epidemiological studies [11] - [14]. Figure 1 illustrates the evolution of the W/Mgender ratio as a function of age and shows that the male subject is more exposed to the cholelithiasis disease at the ends of life.

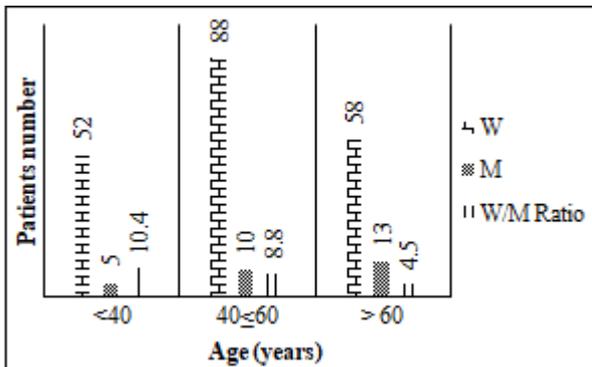


Figure 1: Distribution of patients by age and gender (W: women, M: men)

3.2. Patient distribution by geographical origin and water quality

The results of the patient distribution by geographical area and water quality are graphically illustrated in Figure 2. We studied the presence of cholelithiasis in the region of Beni-Mellal according to the geographical area, in the entire study population. The result is so that 31% of patients live in urban areas (U) and 69% in rural areas (R).

A less quality water has impacts on the human body, when some elements in the water present a concentration higher

than the recommendations for the quality of drinking water. We have identified water quality in 226 patients in the Beni Mellal area. Globally, 30% of the patients use treated water (TW) and 70% use untreated water (UTW).

According to these results, there is a strong correlation between the patients geographical origin and the quality of the water that they consume. This can be explained by the fact that in rural areas, there is a lack in the treatment of drinking water.

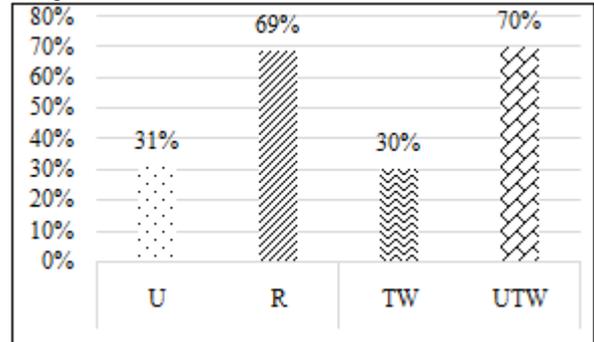


Figure 2: Distribution of patients according to geographical origin (U: urban, R: rural) and water quality (TW: treated water, UTW: untreated water)

3.3. Distribution of patients according to daily water intake (L / D)

Water is the main constituent of living beings and represents about 60% of their organism weight. In fact, the organism needs to renew some water quantity in order to stay well hydrated. This shows that the patient must take care to increase the daily ration so that it is almost 2.5 to 3 L per day [15]. The figure 3 illustrates the obtained results according to the survey that we have carried out. The results show that 96% of patients consume a water quantity note exceeding 2L per day (Figure 3). However, the results show that individuals consuming 2.5L per day also present the cholelithiasis disease. This can be explained by the fact that these disease depends on other parameters such as the consumed water quality (presence of infectious agents, toxic chemicals), the nature of the diet and the drugs. Indeed a high calorie diet, too fat, leads to a high blood cholesterol concentration.

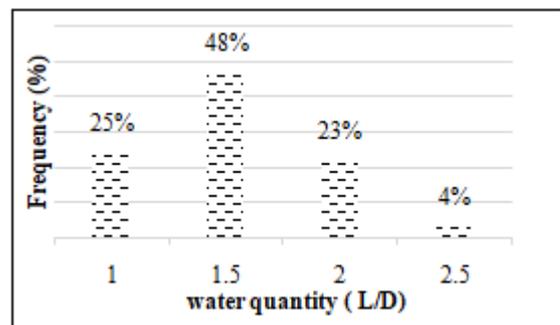


Figure 3: Distribution of patients by daily water intake (Liter/Day (L / D))

3.4. Distribution of patients according to diabetes - and high blood pressure disease

The figure 4 shows the distribution of diabetic patients and arterial hypertension according to gender. The present work

concerned diabetic patients and arterial hypertension patients. Among the total 226 patients in the studied population, 61 patients are diabetic and the other 30 patients present arterial hypertension.

The 61 diabetics population was relatively predominantly female, representing 61% of the total population. The W/M gender ratio was 1.6. Indeed, such a result is comparable to the characteristics of a population that has been studied by Mbarki et al [16].

The population represented by the 30 arterial hypertension patients was predominantly male, accounting for 57% of the total population. The W/M gender ratio was 1.3. Such a result is, also, very close to the characteristics of the population that has been studied by G. Kusuyi Mabele [17].

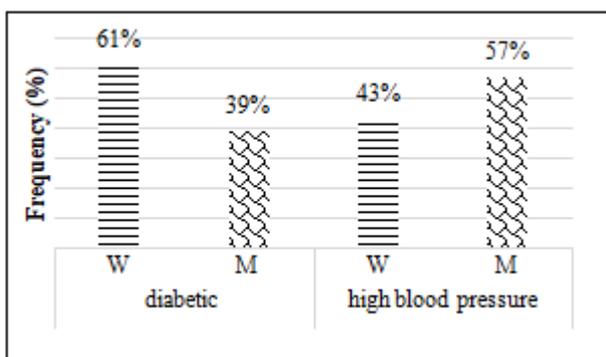


Figure 4: Distribution, of diabetic - and high blood pressure disease, according to gender

3.5. Distribution of patients by family history

Of the 226 studied cases, 36 patients reported similar cases in their families, ie only 15.9%. Indeed: 9 cases of patients are men and 27 cases are women. Family history consists of information about disorders that have been lived by the patient's direct relatives.

The existence of a family antecedent is a risk factor in its own right even in the absence of any inherited vitreoretinal abnormality. This explains the influence of marriages between members from the close family, hence the transmission according to the laws of genetics that is due to one or more abnormalities on one or more chromosomes. In fact, such abnormality causes a malfunction of some cells in the body.

3.6. Distribution of patients by type of the gallstone

According to the analysis of the gallstone shown in figure 5, we note that in the one hand 45% of the patients have showing all stones presenting a core, on the other hand 55% have shown gallstones without core, so that:

- Concerning women: 42% of the total population developed gallstone presenting core (WCG), and 45% developed a no core gallstone (WNCG)

- Concerning men: 3% of the total population developed of gallstone presenting core (MCG), and 10% developed the no core gallstone (MNCG)

Figure 6 shows the distribution of patients presenting core gallstones. It is noted that gallstones presenting a core are rarely observed before the 40 years age so that the frequency is 9% but more observed in the patient whose age exceeds 40 years so that the frequency is 81%. This result can be explained by the fact that the core formation will develop according to the patient age. In addition, the presence of a core in a gallstone can be easily observed thanks to the differences in color and hardness of the gallstone.

3.7. Distribution of patients by type of the cholecystitis

The results of the polarizing light optical microscopy of the gallbladders are illustrated in terms of frequency and types of cholecystitis according to gender and the patients age (Figure 7 and 8). The most common type of cholecystitis for both genders is acute gallstone cholecystitis. Moreover, it is more dominant for all age groups.

The results show that 5.3% of patients presented with a simple gallstone vesicle presenting no sign of malignancy, while 94.7% correspond to complicated cases. Indeed, such a difference to the characteristics of the population that has been studied by S. Benrahhal [12].

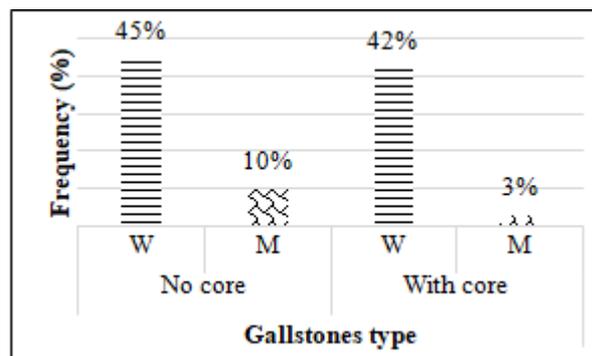


Figure 5: Distribution of gallstones type (no core and presenting core) according to gender

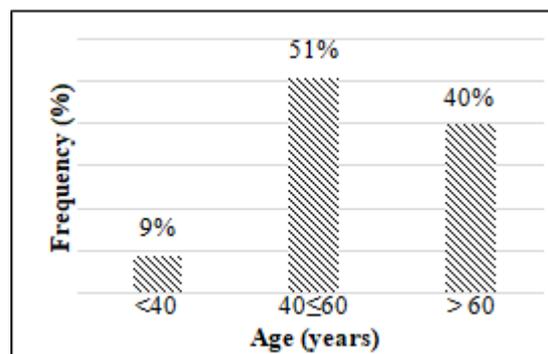


Figure 6: Distribution of gallstones type, presenting a core, by age group

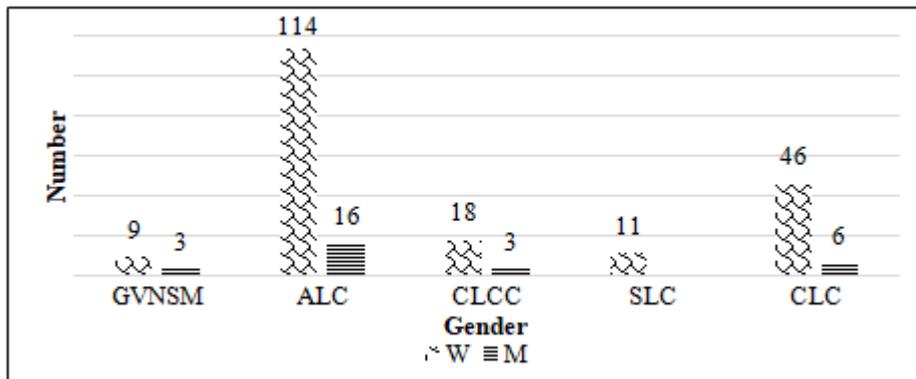


Figure 7: Distribution of gallbladder type according to gender (total population (n =226) (n = 28 in men (M); n = 189 in women (W)). (GVNSM: gallstone vesicle with no sign of malignancy, ALC: acute lithiasic cholecystitis, CLCC: chronic lithiasic cholecystitis with cholesterol, SLC: Simple lithiasic cholecystitis, CLC: Chronic lithiasic cholecystitis)

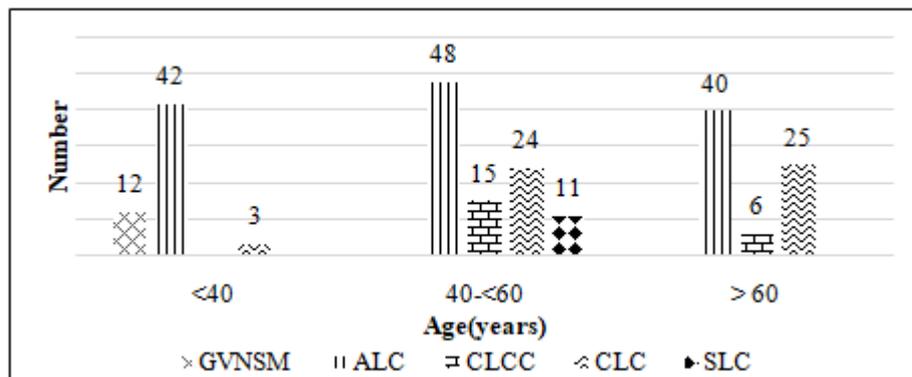


Figure 8: Distribution of gallbladder type according to age group

Acute lithiasis cholecystitis (ALC) is a common condition accounting for nearly one third of surgical emergencies [18]-[19]. It is associated in more than 90% of cases with vesicular lithiasis [18] - [20]. This disease would be present in 10 to15% of the general population [18] - [21] - [22]. Previous studies have shown that the development of vesicular lithiasis and cholecystitis are strongly age-related [18] - [23] - [24]. Patients suffering from the acute cholecystitis present with severe pain that worsens for several hours (usually more than 5 hours), radiating to the interscapular space or right shoulder, accompanied by fever and often nausea and vomiting. Pain in the upper right (but not left) quadrant associated with a palpation defense (Murphy's sign) has high specificity and sensitivity for diagnosis [25].

Chronic lithiasic cholecystitis (CLC) is a longstanding inflammation of the gallbladder, almost always due to gallstone disease. Chronic inflammation of the vesicular wall is almost always associated with the presence of stones and is likely the result of repeated episodes of acute or subacute

cholecystitis or persistent mechanical irritation of the vesicular wall.

Cholesterol gallstones are formed by crystallization of bile cholesterol from a cholesterol-saturated bile that induces an increase in the secretion of mucus by the vesicle, a factor of pro-nucleation of stones. The saturation of the bile in terms of cholesterol chemical species can be direct or consequence of a relative deficit in bile salts by abnormality of the enterohepatic cycle [26].

Simple lithiasis cholecystitis (SLC) is an intermediate type between CLC and ALC so that it is called Subacute lithiasis cholecystitis. It results from the Rokitansky-Aschoff sinus rupture in the vesicular wall that is responsible for parietal infiltration by the bile and the mucin. This infiltration causes a histiocytic reaction that lead to a fibro-oedematous reaction containing insoluble cholesterol favoring the formation of xanthogranulomas within the wall [27].

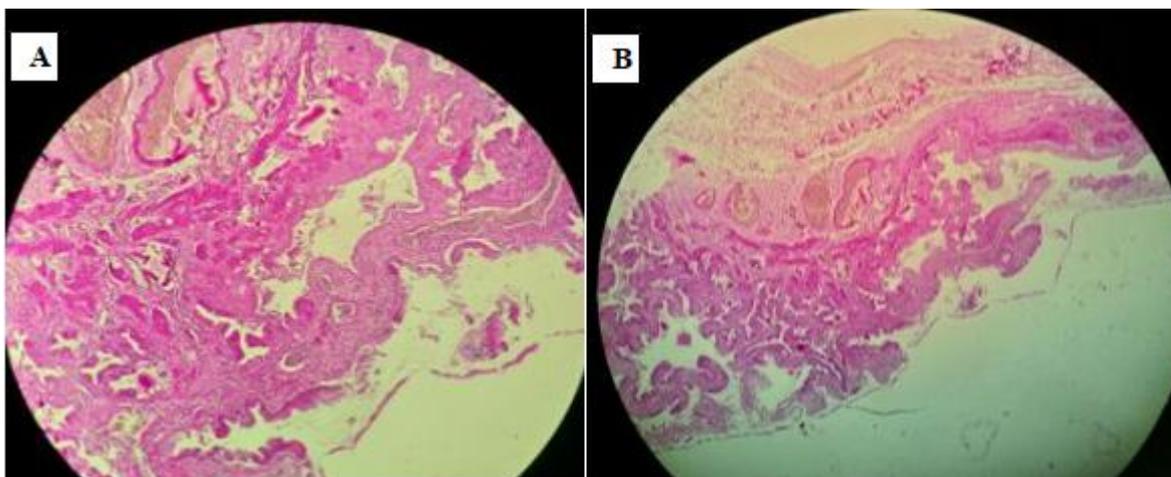


Figure 9: A: Chronic lithiasic cholecystitis with cholesterol (×200), B: Chronic lithiasic cholecystitis (×200)

3.8 Principal component analysis (PCA)

From the figure 10 that represents the score plot of the individuals we can confirm that these individuals are shared in two classes.

In fact, the two classes do not seem to be based on either the gender- or the age factor. However, the first factorial axis

PC1 explains, at best, the influence of the age factor on cholelithiasis. This factorial axis explains the quasi-totality of the information coming from all the eight factors studied. Such results confirm that cholelithiasis disease is a multiple disease.

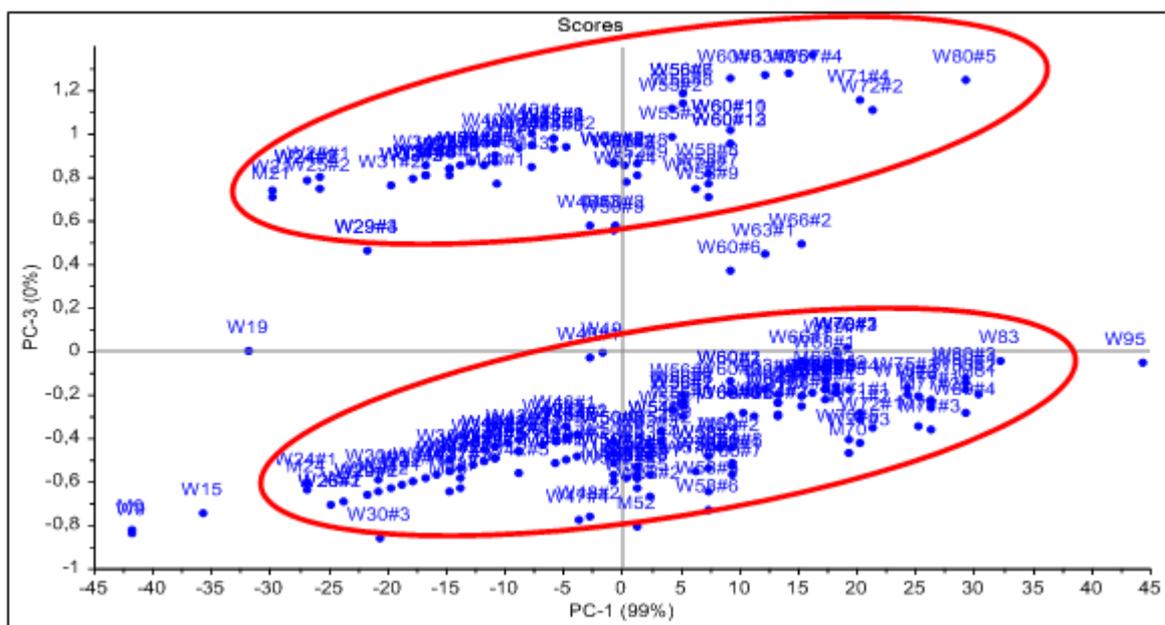


Figure 10: Score plot of the patients according to variables (PC1-PC3)

The figure 11 illustrates the results of the eventual correlations between diabetes disease on the one hand and that of arterial hypertension on the other hand, in lithiasic patients. There is a positive correlation between the two types of diseases. There is a remarkable positive correlation between this type of disease on the one hand and the

frequency of development of the cholelithiasis whose gallstones have a core. In addition to a fluid intake whose water quality is not assured presents a risk that would promote the development of gallstone around this core.

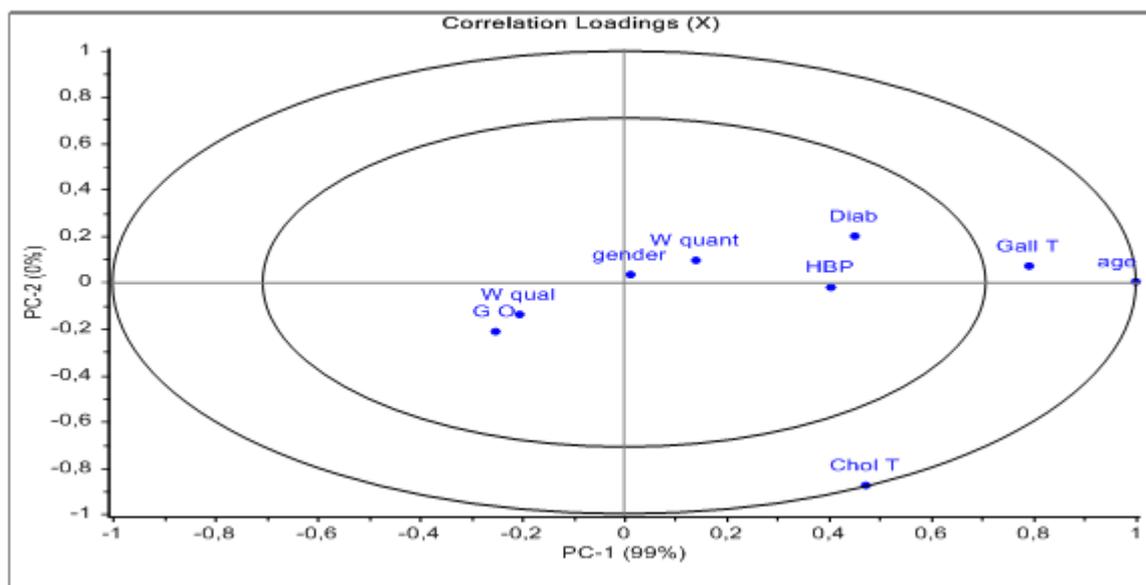


Figure 11: Circles of correlations, in the PC1-PC2 factorial plan, between variables (**Gender**, **Age**, **GO**: geographic origin, **W quant**: Water quantity, **W qual**: Water quality, **Diab**: Diabetes, **HBP**: high blood pressure, **Chol T**: cholecystitis type, **Gall T**: Gallstone type)

4. Conclusion

The present work had, as a main objective, the study of the influence of some parameters on the presence of cholelithiasis in the Moroccan Beni Mellal-Khénifra area.

The gallstone pathology is a multifactorial disease since several factors would have an impact.

Descriptive epidemiological studies have shown that the distribution of cholelithiasis would be influenced by age, gender, ethnicity, obesity and other factors.

The age- and gender factors would have less impact than those detected in diabetes and high blood pressure disease. Some positive correlation between these diseases on the one hand and the formation of core gallstone has been noted. There is a strong correlation between the quality of drinking water on the one hand, and the type of cholelithiasis from, on the other hand.

References

- [1] L. Jean, M. Fabrice, V. Éric, E. Olivier, P. Gilles. "Biliary lithiasis". *Presse Med.* 2011, 40: 567–580.
- [2] V.G. Agadzhanov, A.M. Shulutko, A.M. Kazaryan. "Surgery of the main cholelithiasis by mini laparotomy". (2013) 150, 147–153.
- [3] Spelsberg FW, Nusser F, Huttl TK, et al. "Management of cholecysto- and choledocholithiasis—survey and analysis of 16,615 cholecystectomies and common bile duct explorations in Bavaria". *Zentralbl Chir* 2009, 134(2):120–6.
- [4] R. Amato, K. Pautrat, M. Pocard, P. Valleur. "Surgical laparoscopic treatment of the lithiasis of the main bile duct". 2015.
- [5] BVM. Dasari, CJ. Tan, KS. Gurusamy, et al. "Surgical versus endoscopic treatment of bile duct stones". *Cochrane Database Syst Rev* 2013, 12:CD003327.
- [6] LM. Brown, SJ. Rogers, JP. Cello, KJ. Brasel, JM. Inadomi. "Cost-effective treatment of patients with symptomatic cholelithiasis and possible common bile duct stones". *J Am Coll Surg* 2011, 212(6):1049–60 [e1–7].
- [7] A. Desbeaux, F. Hec, S. Andrieux, A. Fayard, R. Bresson, M.H. Pruvot, E. Mulliez. "Prévention of cholelithiasis and its complications after bariatric surgery". (2010) 147, 278–281.
- [8] A. Bocquier, S. Boullu-Ciocca, P. Verger, C. Oliver. "Obesity: where are we?". *Presse Med* 2006, 35:270–6.
- [9] B. Vastag. "Obesity is now on everyone's plate". *JAMA* 2004, 291(10):1186–8.
- [10] S. Erlinger. "Gallstones in obesity and weight loss". *Eur J Gastroenterol Hepatol* 2000, 12(12):1347–52.
- [11] S.L. Benrahha. "Management of cholelithiasis at Ibn Tofail Hospital in Marrakech" (thesis). 2018.
- [12] JW. Thomas, NL. Dileep. "Gallstones". *Surgery (Oxford)* 2009, 27, 1: 19–24
- [13] C. Buffet, E. Jacquemin, S. Erlinger. "Physiopathology, epidemiology and natural history of cholelithiasis". *EMC Hépatologie* 2008, A10 :4-47. Buffet C, Jacquemin E, Erlinger S.
- [14] S. Erlinger. "Biliary lithiasis". *Gastroentérologie Clinique et Biologique* 2002, 26:1018-25.
- [15] T. Ivan, H. Pascale, F. Marc. "Does drinking enough water protect our kidneys". *Cahiers de nutrition et de diététique* (2016).
- [16] M. Mbarki, J. Jabrane, A. Oussama, M. Daudon. "Study of the crystalluria of diabetic subjects". *Progrès en Urologie.* 2005, 15 (3): 420-426.
- [17] G. Kusuayi Mabele, C. Nkiama Ekisawa, C. Delecluse, F. Lepira Bompeka, A. Nkodila Natuhoyila. "Assessment of the prevalence of high blood pressure in adults in the workplace in Kinshasa, Democratic Republic of Congo". 2018.
- [18] C.S. Loozen, B. van Ramshorst, H.C. van Santvoort, D. Boerma. "Acute cholecystitis in elderly patients: justification for early cholecystectomy". 2017.02.003.

- [19] JD.Browning, JD.Horton. "Gallstone disease and its complications". *Semin Gastrointest Dis* 2003, 14:165—77.
- [20] Y. Kimura, T. Takada, SM. Strasberg, et al. "TG13 current terminology, etiology, and epidemiology of acute cholangitis and cholecystitis". *J Hepatobiliary Pancreat Sci* 2013, 20:8—23.
- [21] EA.Shaffer. "Epidemiology and risk factors for gallstone disease: has the paradigm changed in the 21st century *Curr Gastroenterol Rep*". 2005, 7:132—40.
- [22] S.Tazuma. "Epidemiology, pathogenesis, and classification of biliary stones (common bile duct and intrahepatic)". *Best Pract Res Clin Gastroenterol* 2006, 20:1075—83.
- [23] BD.Schirmer, KL.Winters, R.Edlich. "Cholelithiasis and cholecystitis". *J Long Term Eff Med* 2005, 15:329—38.
- [24] JY. Cho, H.Han, Y.Yoon, KS.Ahn. "Risk factors for acute cholecystitis and a complicated clinical course in patients with symptomatic cholelithiasis". *Arch Surg* 2010, 145: 329—33.
- [25] RL.Trowbridge, NK. Rutkowski, KG. Shojania. "Does this patient have acute cholecystitis?". *JAMA* 2003, 289:80—86.
- [26] P. Sophie. "Pathology of the gall bladder and extrahepatic biliary ducts case 2 and 3 chronic cholecystitis". 2014.06.007.
- [27] C. Isabelle Boulay-Colleta, O. Lucidarme. "Pathologies of the gallbladder, Ultrasound in digestive pathology". Chapter 6, 157-189, 2017 Elsevier Masson SAS.