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DOES HISTOPATHOLOGICAL EXAMINATION STILL HAVE VALUE IN DETECTING AND PREVENTING CANCER?

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ABSTRACT | Introduction: Cancer is a very dangerous disease causing a high mortality rate every year. The prevention or reduction of malignant disease required early detection, mainly depending on histological examination as the first step in the diagnosis. **Methods:** This study was designed to gauge the value of the numbers of histological specimen as an indicator for the level of education to prevent cancer development. Histological specimens of 14670 suspected cases of cancer diseases were histopathologically examined during seven years. **Findings:** Histopathological examination revealed that 960 patients had a positive result of 38 cancer types, while 13710 patients were clear of any type of cancer. More specimens were received from females, especially in 2014 and the most important organs for diagnosis of cancer, included the gastrointestinal tract (gastro-esophagus, gallbladder, and appendix), skin, lymphoid, and breast. **Discussion:** Increase the education level about the importance of histopathological examination of any suspected specimens is considered the first step in preventing and controlling the distribution of cancer disease. Some cancer types should receive greater attention in the diagnosis by increased use of the histopathological laboratories.

Key words: Neoplasms, Histological examination

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INTRODUCTION

Cancer is a hard effected name in which constantly threatens the lives of people all over the world. It can develop into different types of human tissue and at any locations. Thus, any abnormal tissues should be kept under review, even it has changed insignificantly. The histopathological examination is always considered the first step in the detection of cancer disease. More than 300 distinct types of tumors are found that have a developing and progressive course in the patient's body[1]. Therefore, early detection, especially in individuals at high risk will absolutely lead to a better outcome[2]. The significant results in diagnosis of cancer mainly depend on the efficiency of the pathologist who is required to provide an accurate, specific and sufficiently comprehensive diagnosis[1]. The shape and size of cells, their nuclei, and their distribution are the most important microscopical features useful for the pathologist for diagnosis of cancer[3]. However, the accuracy of cancer diagnosis by a pathologist will give a good recommendation to the physician for making the right decision about suitable treatment. Furthermore, for diagnosis of many cancers, a histopathological examination is obligatory for confirmation, even when other diagnostic methods have failed to discover such types of malignant disease as breast cancer, oral squamous cell carcinoma and many of female genital tract cancers[4-7]. Thus, the histopathological examination should be given a full priority by the surgical and clinician teams for detection of cancer.

As the diagnosis is the first step in the treatment of cancer, the recommendation of the histological examination of any suspicious tissue was evaluated in this study as a useful protocol for early detection of cancer disease.

METHODS

Histological specimens of 14,670 (5806 males and 8864 females) suspected cases of cancer diseases were histologically examined by the members of the histopathology department of Al-Ammam AL-Hussein general teaching hospital of Karbala province from January 2009 to December 2015. The total age range of patients was 0-91 years (mean; 47 years). The number of specimens represented the number of patients when a single specimen was taken from each patient. The results of specimen examination were divided into positive and negative results according to the presence or absence of cancer. The specimens were collected from different parts of the patient's body by surgical excision or by use of specific instruments as a biopsy. All biopsies obtained by fine-needle aspiration were eliminated due to their representing a cytological specimen.

Statistical analyses

The data were expressed as mean ± Standard Deviation (SD). Comparison between the number of patients and the total number and between male and female were made using the Student t-test. The value $p < 0.01$ was considered as statistically significant.

RESULTS

The examination of histological specimens of 14670 patients with suspected cancer revealed that 960 patients (412 males and 548 females) had a positive result for 38 cancer types, while 13710 patients (5394 males and 8316 females) were cleared from any type of cancer. Although the received specimens were large in number, it showed a random geometric progression over all periods. The number was largest in 2014, followed by 2012, 2015, 2011, 2010, 2009, and 2013, respectively (Fig. 1.a). The total number of tissue specimens from females was greater than from males during all of the periods, except in 2015 (Fig. 1.a).

The five most frequent cancers investigated in each year showed a variable pattern. Gastro-oesophageal cancer was usually among the most common. In 2009, the five largest numbers of tissue specimens were examined for diagnosis of skin cancer, breast cancer, gallbladder cancer, appendix cancer and gastro-oesophageal cancer, respectively (Fig. 2.a), while the pattern was changed in 2010 and 2011 as follows, gastro-oesophageal cancer, appendix cancer, skin cancer, gallbladder cancer, and breast cancer (the last one replaced by thyroid

cancer in 2011), respectively (Fig. 2.b, c). In the third year (2012), the five most frequent specimens were sent to the laboratory for diagnosis of appendix cancer, gastro-oesophageal cancer, skin cancer, gallbladder cancer, and breast cancer, respectively (Fig. 3.a), while the number increased for diagnosis of gastro-oesophageal cancer, gallbladder cancer, skin cancer, thyroid cancer, and breast cancer, respectively, in the fourth year (2013) (Fig. 3.b). Furthermore, the most common cancer types in received specimens during the last two years (2014-2015) included gastro-oesophageal cancer, skin cancer, breast cancer, colorectal cancer, gallbladder cancer, and lymphoma (Fig. 3.c and 4). Overall, more histological specimens were collected from females, while gastro-oesophageal and colorectal specimens were mostly collected from males (Fig. 1.b). Meanwhile, the less common cancers that showed a variable ranking over all periods in both genders were pancreatic cancer, hemangioma, cecum cancer, intraocular cancer, urethral cancer, brain cancer, head and neck cancer (Fig. 2-4).

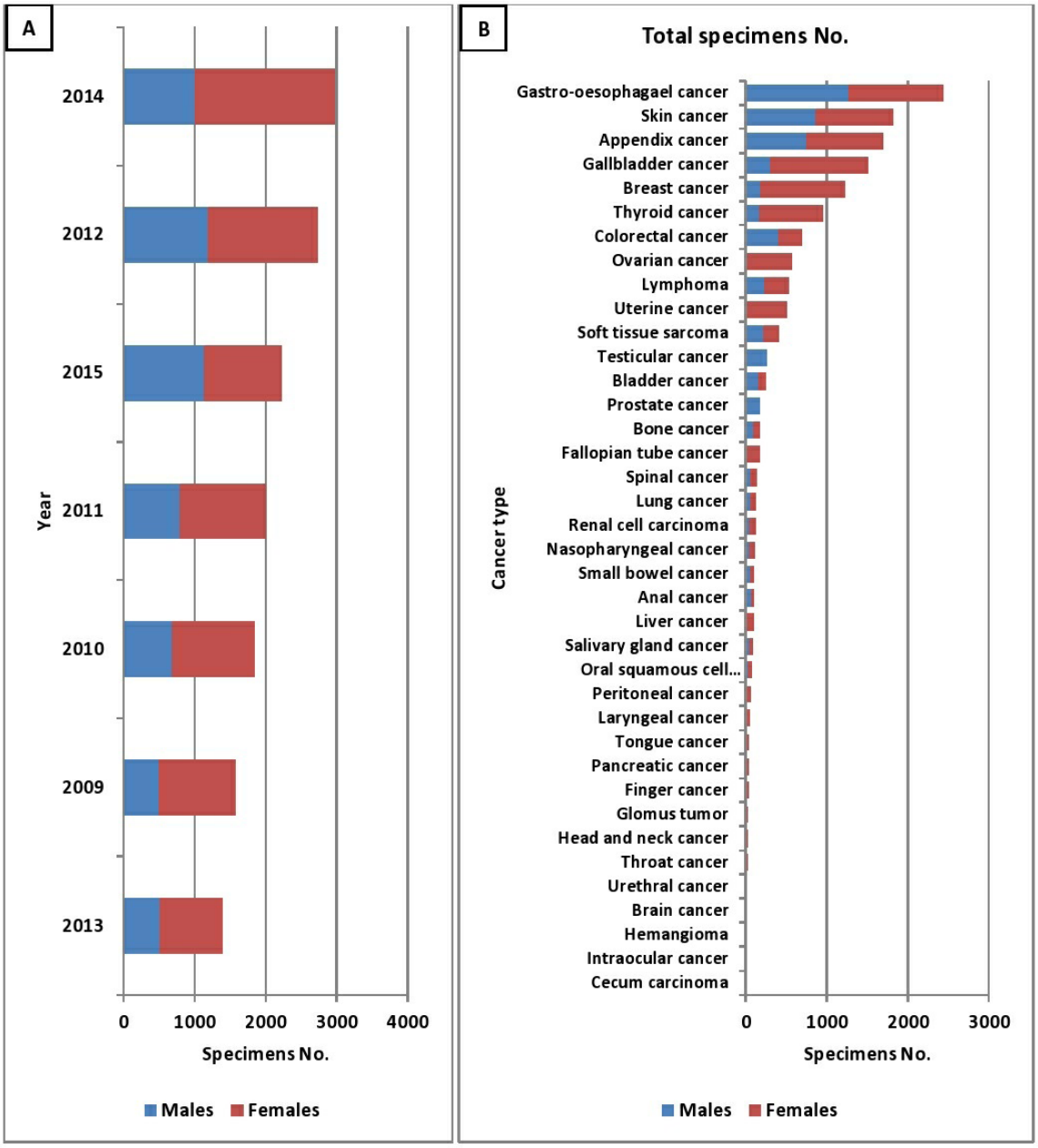

Fig. 1: A total count of histological specimens over all periods.
A: A total count of histological specimens of patients (males and females) in each year.
B: A total count of each type of cancer over all periods.

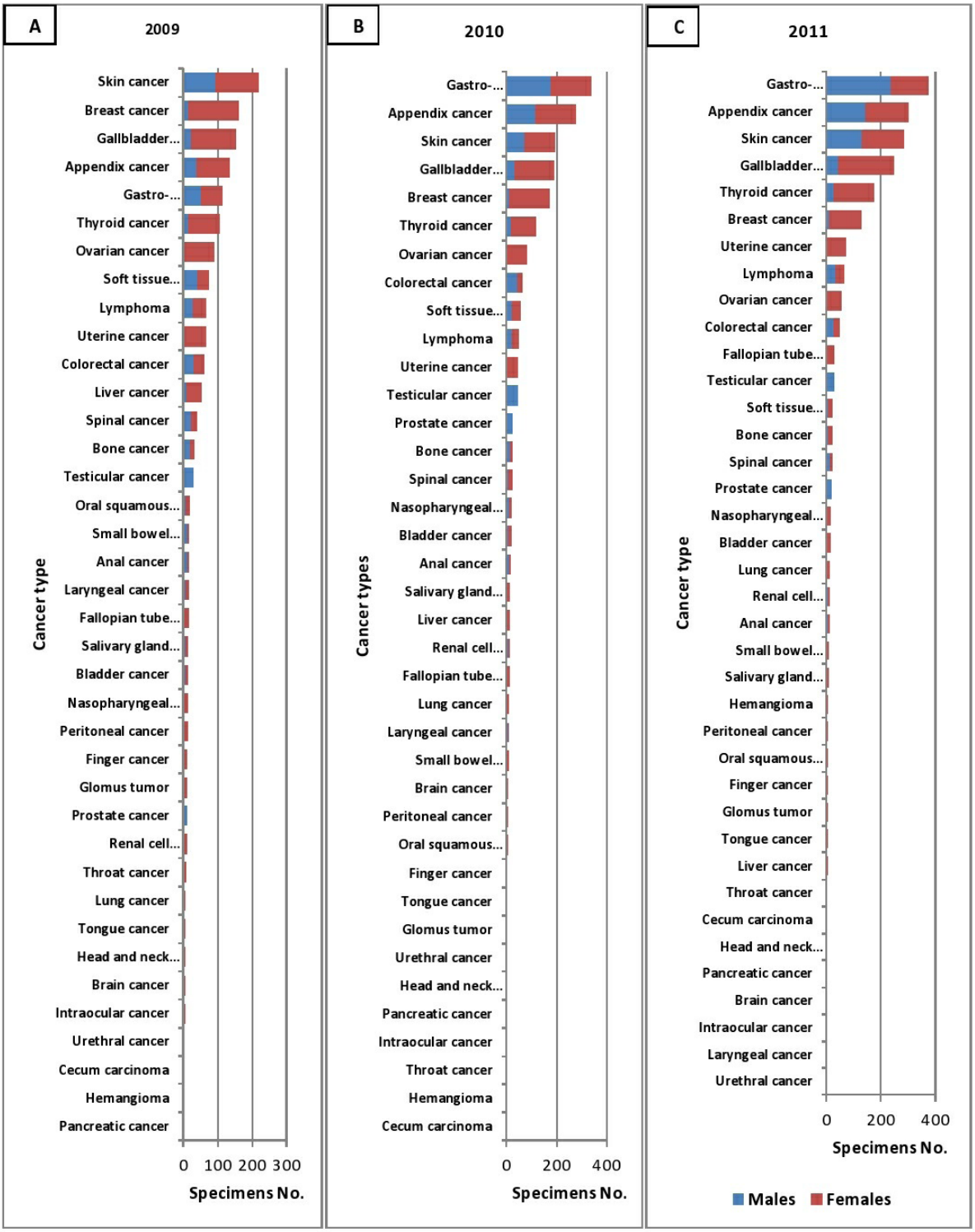

Fig. 2: A total count of histological specimens of patients in each year.
A: 2009; B: 2010; C: 2011

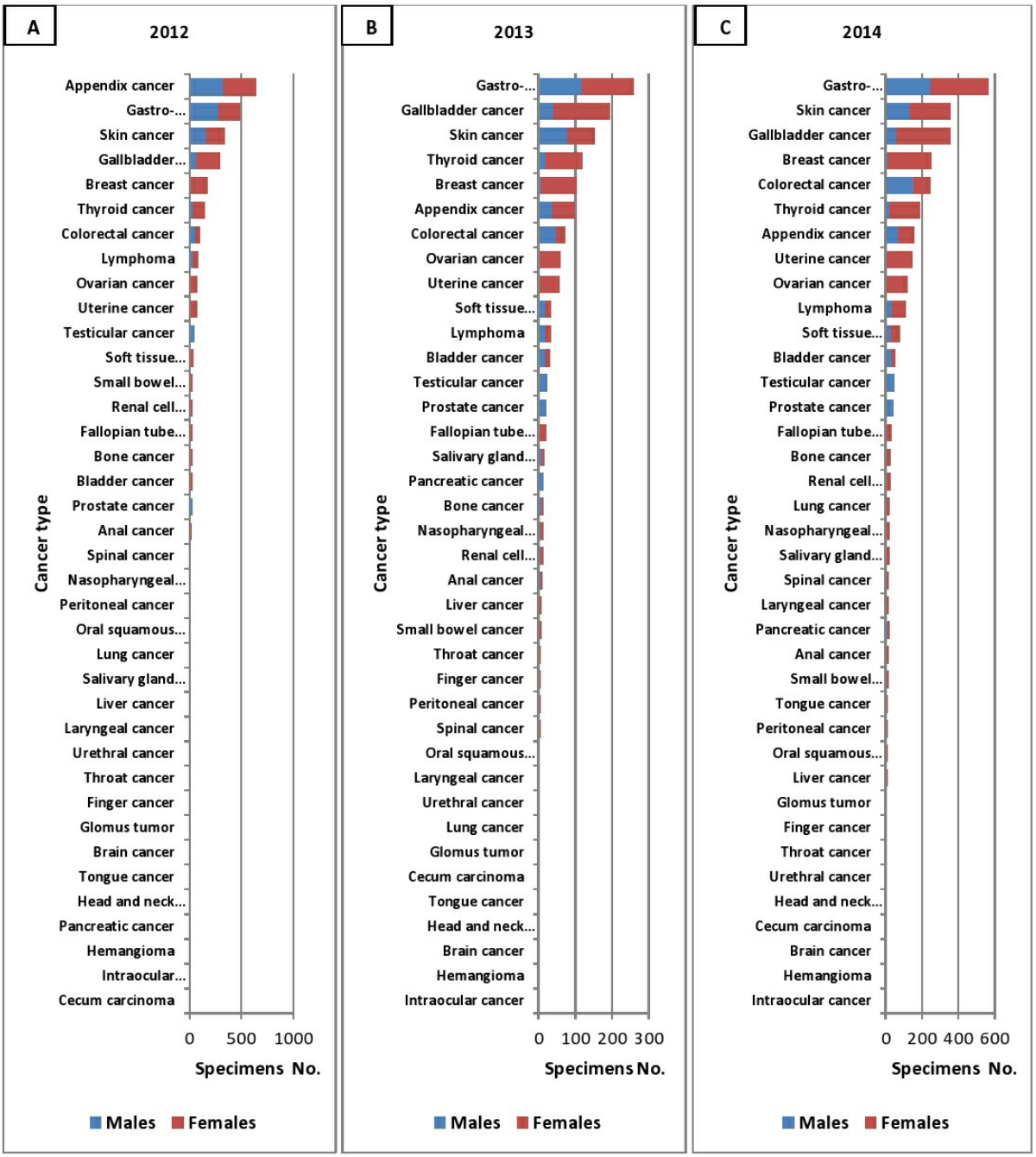

Fig. 3: A total count of histological specimens of patients in each year.
A: 2012; B: 2013; C: 2014

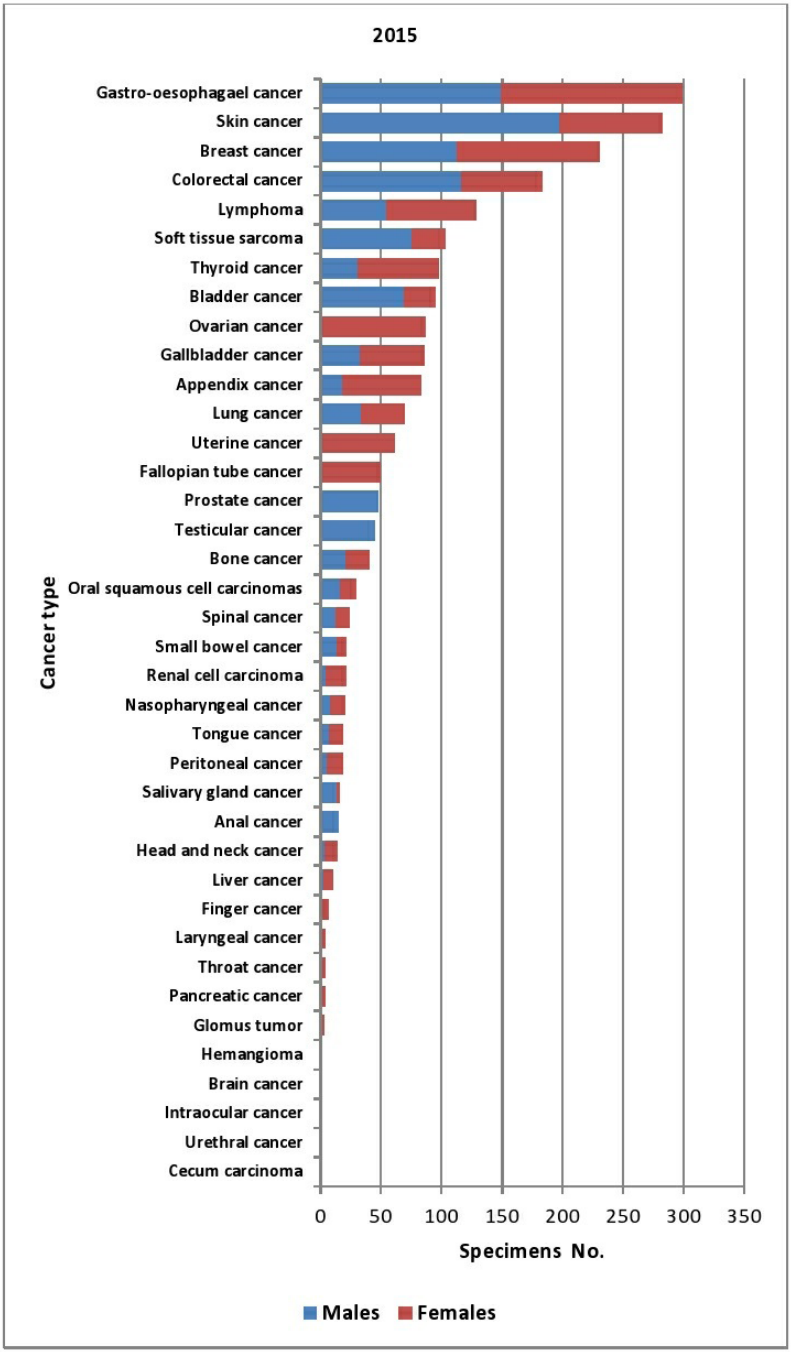

Fig. 4: A total count of histological specimens of patients in 2015.

Generally, the largest number of histological specimens received by the histopathological department over the last seven years was examined for diagnosis of cancer in organs, including that the gastrointestinal tract (gastro-esophagus, gallbladder, and appendix), skin, lymphoid, and breast (Fig. 1.b). Furthermore, high attention was given to the cancers in the organs of the genital tract of females (fallopian tube, ovary, uterus), and males (testis and prostate) (Table 1)(Fig. 1.b). Meanwhile, over the period of seven years, the five most common types of cancer that gave a positive result, included bladder cancer, skin cancer, gastro-oesophageal cancer, colorectal cancer, and lymphoma, respectively, in males and breast cancer, skin cancer, thyroid cancer, lymphoma, and colorectal cancer respectively, in females over (Table 1).

Table (1): The examination results of the histological specimens for diagnosis of different types of cancer during seven years

No.	Cancer type	Males			Females			Total (Males & females)
		Positive Results	Negative Results	Total	Positive Results	Negative Results	Total	
1	Gastro-oesophageal cancer	55±11 [b]	1217±23 [a]	1272	21±4	1140±45 [a]	1161	2433
2	Nasopharyngeal cancer	5±2	43±9	48	4±1.9	57±11	61	109
3	Oral squamous cell carcinomas	4±1.2	34±10	38	5±2	32±7	37	75
4	Tongue cancer	1±0.4	14±4	15	2±0.6	24±5 [b]	26	41
5	Thyroid cancer	12±2	157±20	169	52±8 [b]	727±26 [b]	779	948
6	Salivary gland cancer	5±1.1	43±8	48	7±2	34±2.9	41	89
7	Throat cancer	2±0.7 [b]	7±1	9	0	11±3	11	20
8	Laryngeal cancer	2±0.9 [b]	28±2.4	30	0	21±2.2	21	51
9	Head and neck cancers	2±1	6±1.7	8	1±0.3	13±2 [b]	14	22
10	Small bowel cancer	7±2	51±2 [b]	58	7±2	36±9	43	101
11	Pancreatic cancer	2±1 [b]	28±1.9 [b]	30	0	7±3.4	7	37
12	Liver cancer	1±0	19±2	20	5±2.1 [b]	69±9 [b]	74	94
13	Gallbladder cancer	5±1 [b]	301±30	306	2±0.3	1205±98 [a b]	1207	1513
14	Colorectal cancer	31±7	459±24 [b]	490	26±8	252±24	278	768
15	Appendix cancer	3±1.5	755±20	758	4±1	930±57	934	1692
16	Cecum carcinoma	0	3±1	3	0	2±1	2	5
17	Anal cancer	6±2 [b]	71±6 [b]	77	0	17±0	17	94
18	Soft tissue sarcoma	20±5	200±11	220	15±3.4	168±35	183	403
19	Brain cancer	0	5±1.9	5	1±0 [b]	6±2	7	12
20	Renal cell carcinoma	15±3	38±2.1	53	16±3	48±9	64	117
21	Finger cancer	0	8±2	8	0	26±6 [b]	26	34
22	Bladder cancer	77±12 [b]	86±7	163	24±3.2	61±3.3	85	248
23	Urethral cancer	1±0 [b]	8±1	9	0	3±1.5	3	12
24	Glomus tumor	0	10±2.6	10	0	16±2.1	16	26
25	Bone cancer	12±3	88±4.5	100	9±2	68±2.3	77	177
26	Peritoneal cancer	1±0.4	22±3.2	23	10±2.1 [b]	29±5	39	62
27	Lung cancer	5±0.7	52±5	57	10±1.8 [b]	57±2.9	67	124
28	Hemangioma	1±0.2	1±0.1	2	3±1	2±1	5	7
29	Intraocular cancer	0	2±0.2	2	1±0.2 [b]	3±1	4	6
30	Spinal cancer	0	63±3.9	63	4±2 [b]	67±2.2	71	134
31	Skin cancer	72±8	796±30	868	53±11	900±56	953	1821
32	Lymphoma	28±4	201±23	229	27±5	271±34	298	527
33	Fallopian tube cancer	0	0	0	0	176±41 [b]	176	176
34	Ovarian cancer	0	0	0	0	550±27 [b]	550	550
35	Uterine cancer	0	0	0	0	489±36 [b]	489	489
36	Testicular cancer	4±0.5 [b]	252±21 [b]	256	0	0	0	256
37	Prostate cancer	27±5 [b]	150±30 [b]	177	0	0	0	177
38	Breast cancer	6±2	176±11	182	239±32 [b]	799±33 [b]	1038	1220
Total		412	5394	5806	548	8316	8864	14670

a: significant differences between patients and total No. at P <0.01 | b: significant differences between male and female at P <0.01
*** Mean ± SD

DISCUSSION

Annually, a high percentage of the population is considered at risk of cancer, worldwide. In 2012, WHO estimated that about 14 million cases of cancer were diagnosed, resulting in 8.2 million deaths[8]. Furthermore, the elevated ratio of cancer among the world population has always taken a symposium path with increasing risk factors. Thus, preventing or limiting cancer is regarded one of the difficult challenges for us and it is actually still out of our control, especially in people at higher risk of developing malignancy[9]. The most important point that makes cancer a very dangerous disease is related to the delay in diagnosis and the absence of specific symptoms. Thus, early detection is considered a first step in preventing the development of such types of malignant disease, and then it can be successfully followed by the provision of suitable treatment. Nowadays, there are many types of diagnostic techniques that can be used for detection of cancer, but unfortunately, they still have a high failure rate, especially for the diagnosis of the early stages. This situation makes the physician and surgeon deal with the enlarged tissue of a range of sizes, and even if small a suspicious case should be sent to the pathologist to get the final decision[2]. Therefore, the number of specimens sent for histological examination is considered a good indicator for the level of education showed by the medical staff, which absolutely leads to limit the mortality rate of cancer[2].

Although many modern techniques are available in most of our medical foundations, the histopathological examination still has a prognostic value in the detection of cancer with more significant results than other diagnostic methods. This depends on many important things about the histopathological examination that is mainly associated with the high accuracy in the diagnosis of cancer as with breast cancer (95.4%) and other types of malignant diseases such as high-grade gliomas[10]. Meanwhile, the examination revealed more significant diagnostic results for many cancers compared with other methods as with a mammography screening for breast cancer[7] or with other laboratory techniques like light-based detection and oral spectroscopy[6]. However, visual examination of tissue can also give a false result as noted with the diagnosis of breast cancer in which the false negative was found to be about 5% to 8% of cases[5] and in about 4.5% of patients with a positive human papillomavirus (HPV) DNA test[11]. The false results found in the pathology report may be related to various reasons, including the efficiency (accuracy) of the examiner when the cancer is difficult to diagnose as with squamous lesions in the uterine cervix[12] and the degree of precision with which depending on the examination is reproducible[13]. However, delay in diagnosis by a pathologist is attended by many problems that relate to either a pre-laboratory step as with taking an adequate sample, labeling, and arrival in the laboratory; in the laboratory so as to delay completion of the report that may lead to delay in the treatment; post-laboratory step such as the failure to receive the results[1,14]. Thus, other methods or techniques may be required to increase the diagnostic value of histopathological results as the use of immunohistochemistry for cytokeratin, biochemical analysis, computer-assisted diagnosis and optical imaging in vivo[5,15-17]. Furthermore, repeated examination or increasing the number of the excision and/or biopsy specimens to more than one will decrease the errors.

The biopsy, especially the excisional biopsy, is the perfect specimen for histopathological examination[1,18]. It usually arrives in the laboratory in a preservative solution or as frozen sections[5,19]. The excision often includes the tissue surrounding of the malignant lesions[20] and it can be repeated more than once for some types of cancer such as pancreatic cancer[21]. However, the character of the whole structure of the specimen, followed by the visual examined is the principal step used by pathologists in the diagnosis of the abnormal tissue[1]. In addition, the cytological examination has also played an important role in the diagnosis of cancer[4], and its results could be helpful for confirming of the histological examination[13,22]. Although the cytological analysis has many disadvantages[23-24], it also has several benefits compared with the pathological analysis, including cost-effectiveness, rapid turnaround time, providing a minimal risk for the patient, and giving the results when other techniques failed[1,4].

The histopathological examination supplies more advantages for diagnosis of cancer than other methods. The first one is the accuracy in detection of cancer compared with that obtained with other

methods[4,6-7,10] and the ability to differentiate between benign and malignant disease[18,25]. Furthermore, the assistance of other methods for detection of cancer is another benefit of histopathological examination as it increases the sensitivity of PSA in the detection of the prostate cancer[26] or preliminary diagnosis of basal cell carcinoma based on the appearance[20]. The treatment also depends on the results of the pathologist´s report, especially after determining the stage of cancer in the patient's body[1]. Furthermore, the greatest benefits provided by histopathological examination is determined of the classification scheme of cancer, which depend on the tumors gross morphology, the degree of cellular differentiation and the tumor´s histogenic or cytogenic origin[1,27].

In addition to the above benefits that obtain from the histopathological examination, it also provides useful data for epidemiological studies about cancer in any region of the world[27]. The recent results of cancer incidence in only one city (Karbala) in Iraq showed that the GIT organs developed the most common cancers over all periods of study. Meanwhile, a huge number of tissue specimens were examined for diagnosis of genital tract cancers in males (testicular cancer and prostate cancer) and fallopian tube cancer, ovarian cancer and uterine cancer in females, followed by the soft tissue sarcoma and breast in males and thyroid cancer with skin cancer in females. On the other hand, more than 25 types of cancers were given little attention during the same periods as indicated by the small number of histological specimens received by the histopathological lab. These results can give us two main conclusions. First, the diseases in some organs of people living in Karbala city were more frequent than other regions and this would increase the possibility of cancer development. Second, the large number of histological specimens received by the laboratory indicated the presence of a high level of education among the medical staffs (physicians and surgeons) who directly deal with patients about the importance of discovering and preventing the development of cancer or its metastasis. However, the number of the specimens for diagnosis of cancer was expected to rise within the time considered as we assume that the education level about the risk of cancer now is higher than that in the past, but we cannot assure this affirmative. The best explanation for that is the medical staff often changed their work place between the Iraqi cities, which affected the results of the application of cancer prevention program. Thus, it is necessary to design a program that can deal with this problem.

CONCLUSION

Increase in the education level about the importance of histopathological examination of any suspicious specimens, even of insignificant size, is considered the first step in preventing and controlling the distribution of cancer disease. Some cancer types should be given more attention in their diagnosis by increasing the sending of histological specimens to the histopathological laboratories.

COMPETING INTERESTS

No financial, legal or political competing interests with third parties (government, commercial, private foundation, etc.) were disclosed for any aspect of the submitted work (including but not limited to grants, data monitoring board, study design, manuscript preparation, statistical analysis, etc.).

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