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Study the effect as risk factors, examination & treatment methods, and extent of health awareness of doctors and patients on the prevalence of pancreatic cancer in Iraq.

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بسم الله الرحمن الرحيم

يرفع الله الذين آمنوا منكم والذين أوتوا العلم درجات والله بما تعملون خبير

صدق الله العلي العظيم

الاهداء

-الحمد لله حبا وشكرا وامتنانا على البداية والختام .

لم تكن الرحلة قصيرة ولا الطريق محفوفًا بالتسهيلات، لكنني فعلتها، فالحمد لله الذي يستر البدايات وبلغنا النهايات.

أهدي هذا النجاح لنفسي الطموحة أولاً .. ثم إلى كل من سعى معي لاتمام مسيرتي الجامعية.

-إلى اليد الخفية التي أزالت عن طريقي الأشواك ومن تحملت كل لحظة الم، مررت بها وساندتني وسهرت ليالي طويلة

من أجل راحتي واستيقظت فجرا للدعاء لي.. إلى (أمي الحبيبة)

-إلى من احمل اسمه بكل فخر ومن دعمني بلا حدود وأعطاني بلا مقابل، إلى من علمني أن الدنيا كفاح وسلاحها العلم

والمعرفة، داعمي الأول في مسيرتي وسندي وقوتي وملاذي بعد الله فخري واعتزازي .. (أبي الغالي)

-إلى من ساندوني بكل حب ووقت ضعفي وأزاحوا عن طريقي كل المتاعب(إلى إخوتي وأخواتي)

-إلى مَن كانوا موضع الاتكاء في كل عثراتي، (إلى أصدقاء العمر)

-إلى أكثر دكتورة تركت بصمة عالية بأخلاقها وتعاونها ومحبتها الإخوية ذات الرقي والأخلاق العالية، أسأل الله كل

التوفيق لها، (د. صفا)

شكر وتقدير

وفي الختام ..... أقف اليوم أمامكم، قلبي يملؤه مزيج من المشاعر المتناقضة، فرحة الإنجاز وحزن الفراق، مشاعر ممزوجة بذكريات رحلة تعليمية طويلة ومليئة بالتحديات والإنجازات

أود أن أتوجه بالشكر الجزيل لكل من ساهم في رحلتي التعليمية، من معلمين وإداريين وأولياء أمور . لقد كانت رحلة مليئة بالتحديات والإنجازات، وكل خطوة فيها كانت تحمل في طياتها دروساً قيمة ستحملها معنا إلى المستقبل.

وأخيراً، أود أن أؤكد على أن هذه ليست النهاية، بل هي بداية جديدة لرحلة أخرى مليئة بالتحديات والفرص ، سنواجه صعوبات جديدة، لكننا ستستمر في السعي لتحقيق أحلامنا وطموحاتنا

Abstract:

Cancer is one of the most prevalent malignant diseases in the world, and despite the efforts to find a cure for this disease, but the disease takes a lot of human lives. Pancreatic cancer is an uncommon tumor, but because the mortality rate approaches 100%, this form of cancer has now become a common cause of cancer mortality, which is the fifth most common in the world, and the cause of death in many Sometimes. The aim of this research is to study the effect as risk factors, examination & treatment methods, and extent of health awareness of doctors and patients on the prevalence of pancreatic cancer in Iraq.

Methods: The study design was a retrospective hospital-based record study in which records of 40 pancreatic cancer patients registered, evaluated, and treated at Iraq cancer control center from November 2024 through March 2024 were studied. This study included an estimation for the levels of some biochemical parameters in the serum of those pancreatic cancer patients, by collecting (40) blood samples from patients their ages ranged (30-90) years compared with (50) blood samples of healthy persons as control group. The parameters included Super oxide dismutase, Amylase, liver function test, kidney function test, lipid profile, carbohydrate antigen 19-9. A questionnaire is used to gather information about the patient and including name, home address, age, sex, height, weight, whether the patient is a smoker, whether he has chronic diseases, history of chronic disease. Also, a questionnaire is used to gather information about the doctor's health awareness of this cancer.

Results: Results of the Statistical analysis indicated forty patients with pancreatic carcinoma were studied, 30(77.78%) patients were males, and 19(22.22%) patients were females, with males to female's ratio of 3:1. Their age range from 30 to 90 years. The commonest risk factor was smoking occurred in 20(44.42%) patients, this was followed by diabetes mellitus occurred in 9(22%) patients. Jaundice was the commonest presenting symptom 32(72%) patients. Most cases were very advanced at time of diagnosis and 30 (87.5%) patient curative Whipple procedure was done. Tumor of the body of pancreas was very much infrequent than the head of pancreas was seen in 6 (13.3%) patients. Results of this study indicated a significant decrease in the activity of Amylase and Super oxide dismutase patients in comparison with the control group. There was a significant increase in liver function test, kidney function test, carbohydrate antigen 19-9, Total lipid in patients in comparison with the control group.

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Introduction

Structure of the Pancreas:

The pancreas is a visceral organ located posterior to a stomach in the form of a leaf. It measures roughly 15 cm in length and 5 cm in width in adults. The pancreas is subdivided into four distinct regions: a head, neck, body, and tail. The head of the pancreas is the broader part, situated adjacent to the stomach and duodenum junction, where the bile duct either lies within a groove on its surface or passes through its substance. The neck and body regions are surrounded by major blood vessels. Finally, the tail of the pancreas is located anterior to the left kidney and spleen [1].

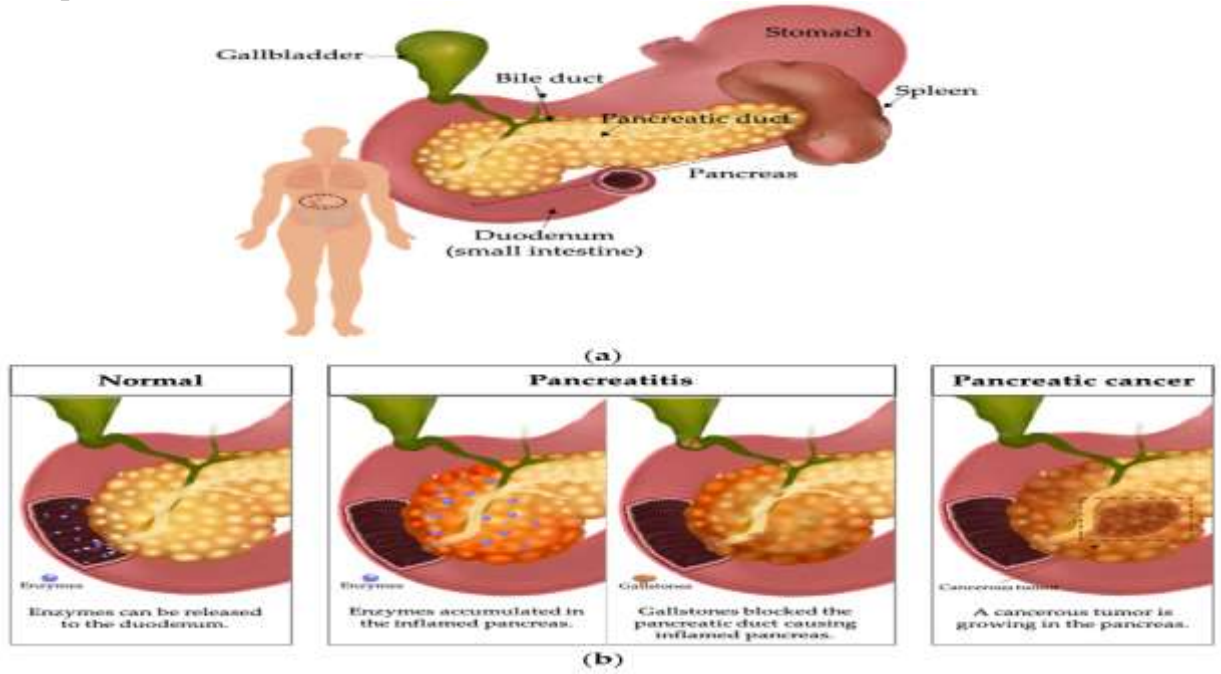

Figure 1 : Structure of pancreas.

Function of the Pancreas

The organ comprises both endocrine and exocrine cells, which perform distinct functions. Most pancreatic cells are exocrine cells, which make up the exocrine glands and ducts. These cells are responsible for secreting a range of enzymes including amylase for carbohydrate digestion, proteases such as trypsin, chymotrypsin, elastase, and carboxypeptidases for amino acids digestion, and lipase for the breakdown of fatty acids. In contrast, the endocrine cells comprise a small proportion of the organ but play a crucial role in the secretion of hormones such as insulin and glucagon, which regulate blood glucose levels by releasing them directly into the bloodstream. The pancreas primarily comprises exocrine cells forming the exocrine glands and ducts [1,2].

Incidence of Pancreatic Cancer

PC represents a frequent contributor to oncological mortality and is distinguished by a high degree of variability, a heavily populated stromal microenvironment within the tumoral mass, an inclination towards extensive metastasis, and a significant reconfiguration of cellular metabolism (see in Figure 1b). Within the realm of PC, malignancies can arise from either exocrine or endocrine cells. The most prevalent form of PC originates from exocrine cells, specifically known as pancreatic ductal adenocarcinoma (PDAC).

Exocrine (Nonendocrine) Pancreatic Cancer

Exocrine pancreatic cancer develops from exocrine cells, which make up the exocrine gland and ducts of the pancreas. The exocrine gland secretes enzymes that help break down carbohydrates, fats, proteins, and acids in the duodenum. The several types of exocrine pancreatic cancers make up more than 95 percent of all cancers of the pancreas [3]. They include the following:

Adenocarcinoma

Also called ductal carcinoma, adenocarcinoma, is the most common type of pancreatic cancer, accounting for more than 90 percent of pancreatic cancer diagnoses. This cancer occurs in the lining of the ducts in the pancreas, and it is a malignancy that has a dismal outcome, with a 5-year overall survival rate of less than 10%, even though the development of the medical treatment [4]. It is also possible for adenocarcinoma to develop from the cells that create pancreatic enzymes. When this occurs, it is called acinar cell carcinoma, which accounts for 1 percent to 2 percent of exocrine cancers. Acinar cell carcinoma symptoms are similar to the symptoms of adenocarcinoma, which include abdominal pain, nausea and weight loss. However, jaundice is not as common. Due to an increase in enzymes, some patients may have skin rashes and joint pain [5].

Squamous Cell Carcinoma

This extremely rare nonendocrine cancer of the pancreas forms in the pancreatic ducts, and is made purely of squamous cells, which are not typically seen in the pancreas. There have not been enough reported cases of this disease for its origins to be fully understood. Studies have reported that it has a very bad prognosis due to most cases being discovered after metastasis. . However, these subtypes are much less common and account for a smaller percentage of PC cases [5].

Adenosquamous Carcinoma

This rare type of pancreatic cancer represents 1 percent to 4 percent of exocrine pancreatic cancers. Compared with adenocarcinoma, adenosquamous carcinoma is a more aggressive tumor with a poorer prognosis. These tumors show characteristics of both ductal adenocarcinoma and squamous cell carcinoma[3].

Colloid Carcinoma

Another rare type, colloid carcinomas account for 1 percent to 3 percent of exocrine pancreatic cancers. These tumors tend to develop from a type of benign cyst called an intraductal papillary mucinous neoplasm (IPMN). Because the pancreatic colloid tumor consists of malignant cells that float in a gelatinous substance called mucin, it is not as likely to spread and is easier to treat than other pancreatic cancers. It also has a much better prognosisNeuroendocrine Pancreatic Cancer[3].

Pancreatic neuroendocrine tumors (NETs)

Pancreatic neuroendocrine tumors develop from cells in the endocrine gland of the pancreas, which secretes the hormones insulin and glucagon into the bloodstream to regulate blood sugar. Also known as endocrine or islet cell tumors, neuroendocrine cancers are rare, making up less than 5 percent of all pancreatic cancer cases [3].
Despite being a relatively uncommon cancer among all malignancies, PC is a leading cause of cancer-related mortality. According to the Globocan 2020 report, it ranks as the 12th most frequent cancer incidence (4.96 million cases), among the top 7 leading causes of cancer-related deaths (4.66 million deaths). The report indicates that there is a higher prevalence of PC among men in comparison to women. Furthermore, this malignancy is more prevalent in countries with high human index (HDI) compared to low HDI countries, and there has been a slight upward trend in incidence and death for two decades [6,7,8,9,10].

Pancreatic Cancer Risk Factors

Pancreas cancer is considered an ‘orphan ’cancer because of its relative low incidence. Unfortunately even with early diagnosis, mortality rates are high, explaining why, despite the low incidence, it ranks eighth in a world listing of cancer mortality. International incidence rates vary in different countries, implying that environmental factors are important. Of these factors, smoking is the most well documented etiologic agent, explaining about 25% of all cases. Dietary factors may be important, but it has been difficult to define specific items which either increase or decrease the risk of pancreatic cancer. Since the incidence of pancreas cancer is so strongly age-dependent, we can anticipate an increasing number of patients as the population of most Western countries ages {11}

1- Risk factors that can be changed
2- Risk factors that can't be changed
3- Factors with an unclear effect on risk

Risk factors that can be changed :

- Tobacco use

Smoking is one of the most important risk factors for pancreatic cancer. The risk of getting pancreatic cancer is about twice as high among people who smoke compared to those who have never smoked. About 25% of pancreatic cancers are thought to be caused by cigarette
smoking. Cigar smoking and the use of smokeless tobacco products also increase the risk. However, the risk of pancreatic cancer starts to drop once a person stops smoking . [12]

- Being overweight

Being very overweight (obese) is a risk factor for pancreatic cancer. Obese people (body mass index [BMI] of 30 or more) are about 20% more likely to develop pancreatic cancer. Gaining weight as an adult can also increase risk. Carrying extra weight around the waistline may be a risk factor even in people who are not very overweight. [13]

Diabetes

Pancreatic cancer is more common in people with diabetes. The reason for this is not known. Most of the risk is found in people with type 2 diabetes. This type of diabetes is increasing in children and adolescents as obesity in these age groups also rises. Type2 diabetes in adults is also often related to being overweight or obese. It's not clear if people with type 1 (juvenile) diabetes have a higher risk.

Chronic pancreatitis

Chronic pancreatitis, a long-term inflammation of the pancreas, is linkedwith an increased risk of pancreatic cancer. Chronic pancreatitis is often seen with heavy alcohol use and smoking.

Workplace exposure to certain chemicals

Heavy exposure at work to certain chemicals used in the dry cleaning and metal working industries may raise a person's risk of pancreatic cancer.

- Risk factors that can't be changed

Age

The risk of developing pancreatic cancer goes up as people age. Almost all patients are older than 45. About two-thirds are at least 65 years old. The average age at the time of diagnosis is 70.

Sex

Men are slightly more likely to develop pancreatic cancer than women. This may be due, at least in part, to higher tobacco use in men, which raises pancreatic cancer risk (see above).

Race

African Americans are slightly more likely to develop pancreatic cancer than whites. The reasons for this aren't clear, but it may be due in part to having higher rates of some other risk factors for pancreatic cancer, such as diabetes, smoking , and being overweight.

Family history

Pancreatic cancer seems to run in some families. In some of these families, the high risk is due to an inherited syndrome (explained below). In other families, the gene causing the increased risk is not known. Although family history is a risk factor, most people who get pancreatic cancer do not have a family history of it.

Inherited genetic syndromes

Inherited gene changes (mutations) can be passed from parent to child. These gene changes may cause as many as 10% of pancreatic cancers. Sometimes these changes result in syndromes that include increased risks of other cancers (or other health problems).

Examples of genetic syndromes that can cause pancreatic cancer include:

● **Hereditary breast and ovarian cancer syndrome,** caused by mutations in the BRCA1 or BRCA2 genes

● **Hereditary breast cancer,** caused by mutations in the PALB2 gene

● **Familial atypical multiple mole melanoma (FAMMM) syndrome,** caused by mutations in the p16/CDKN2A gene and associated with skin and eye melanomas

● **Familial pancreatitis**, usually caused by mutations in the PRSS1
Gene

● **Lynch syndrome**, also known as hereditary non-polyposis colorectal cancer (HNPCC), most often caused by a defect in the MLH1 or MSH2 genes

● **Peutz-Jeghers syndrome,** caused by defects in the STK11 gene. This syndrome is also linked with polyps in the digestive tract and several other cancers. [14]

Chronic pancreatitis (due to a gene change)

Chronic pancreatitis is sometimes due to an inherited gene mutation . People with this inherited (familial) form of pancreatitis have a high lifetime risk of pancreatic cancer [15].
Factors with an unclear effect on risk

Diet
Diets with red and processed meats (such as sausage and bacon) and saturated fats may increase the risk of pancreatic cancer. Sugary drinks may also increase this risk. More research is needed in this area.

Physical inactivity
Some research has suggested that lack of physical activity might increase pancreatic cancer risk. But not all studies have found this . Regular physical activity may help reduce the risk of pancreatic cancer. [16]

Coffee
Some older studies have suggested that drinking coffee might increase the risk of pancreatic cancer, but more recent studies have not confirmed this.

Alcohol
Some studies have shown a link between heavy alcohol use and pancreatic cancer. Heavy alcohol use can also lead to conditions such as chronic. pancreatitis, which is known to increase pancreatic cancer risk. [17]

Infections
Some research suggests that infection of the stomach with the ulcercausing bacteria Helicobacter pylori (H. pylori) or infection with Hepatitis B may increase the risk of getting pancreatic cancer. More studies are needed.

Hyperlinks:

Diagnosis of pancreatic cancer
A diagnosis of pancreatic cancer is based on the results of the following examinations and tests;

Current Examination Circumstance
The asymptomatic nature of PC in its initial stages often leads to a delayed diagnosis until the disease has progressed to a more advanced stage, resulting in a significantly reduced survival rate and affecting the efficacy of current therapeutic options. On the other hand, the mortality rate of other cancers, such as breast cancer, has seen a substantial decline of 43% between 1989 and 2020 due to advancements in diagnostic and screening procedures. Consequently, the importance of early detection in enhancing the prognosis of PC cannot be overstated].18]. As the cancer progresses, the symptoms

experienced can vary depending on the whether the tumour is located in the pancreatic head, body or tail. Tumours in the pancreatic head tend to cause more symptoms than those in the body or tail –this is because tumours in the pancreatic head may press on the bile duct or pancreatic
duct and cause conditions such as jaundice.[19]

• Yellowing of the skin and whites of the eyes (for pancreatic head tumours).
• Abdominal pain.
• Weight loss.
• Fatty stools.
• Symptoms of new-onset diabetes, such as thirst, frequent urination and fatigue

However, it is important to remember that these symptoms can also be experienced by people who do not have pancreatic cancer; they may also be caused by other condition

Imaging Modalities

Imaging techniques have been employed for PC screening patients with clinical symptoms and associated risk factors. A comprehensive imaging assessment, which includes non-invasive methods such as ultrasound, computed tomography (CT), MRI, positron emission tomography (PET), endoscopic retrograde cholangiopancreatography (ERCP), and EUS, is recommended for screening purposes. However, specific imaging modalities may be inadequate in detecting early lesions or distinguishing benign from malignant lesions. Therefore, selecting the appropriate imaging technique depends on the patient's overall health, symptoms, and medical history [20].

Ultrasound

Ultrasound is a non-invasive, cost-effective diagnostic tool frequently used in individuals with jaundice or abnormal pain. Although its accuracy is estimated to be between 50–70%, its sensitivity and accuracy in detecting PC are controversial, with factors such as operator experience, size of the tumor, patient body habitus (adipose tissue), and presence of bowel gas influencing the quality of the image].21]

Although traditional ultrasound has limitations, EUS produces high-quality images and has become a valuable diagnostic tool. EUS uses endoscopy and ultrasound imaging to generate detailed images of the pancreas, even in the case of small tumors (<3 cm) [22,23], without the risk of ionizing radiation associated with CT scans [24]. However, the conventional EUS alone may only sometimes be sufficient, despite its high sensitivity and specificity over cross-sectional imaging fields [25,26]. Therefore, EUS is frequently combined with other methods, such as contrast-enhanced (CE), elastography, fine-needle aspiration (FNA), and fine-needle biopsy (FNB), to improve PC evaluation and avoid misdiagnosing it as pancreatitis.

CE-EUS is a technique that employs high-resolution endoscopic ultrasound waves and intravenous contrast to aid in identifying pancreatic lesions [27]. It is a highly accurate method with a sensitivity of 91% and specificity of 93% [28,29], that can effectively differentiate between lesions caused by pancreatitis and those resulting from PC [30,31]. EUS-elastography is a non-invasive method that employs an ultrasound probe to evaluate the soft tissue's elasticity. Used in conjunction with endoscopic ultrasound fine-needle aspiration (EUS-FNA), this technique can assist in distinguishing between malignant and benign lesions by measuring the velocity of a shearing wave as it passes through the tissue. With a sensitivity of 95–97% and specificity of 67–76%, this technique is suitable for diagnosing PC lesion fields [22,23,25,32], and is becoming another gold standard for PC diagnosis].33]

While the endoscopic procedure with the ultrasound probe is employed for tissue evaluation, ERCP integrates endoscopic techniques with X-ray imaging for diagnostic purposes in bile and pancreatic ducts distinct from the ultrasound-guided sample collection [26]. Additionally, alternative non-invasive imaging methods, including CT and MRI scans, offer superior image resolution for the assessment of pancreatic lesions. These imaging techniques provide enhanced detail and precision in evaluating the pancreatic tumors [26]. Consequently, CT and MRI scans are often considered for PC diagnosis as well.

CT

A conventional CT scan generates sequential three-dimensional images using a rotational and continuous X-ray technique. This method assists in detecting lesions by enhancing the contrast (CT density) between normal tissue and abnormal tumors. Furthermore, multidetector CT (MDCT) presents higher-resolution images and quicker imaging duration compared to conventional CT scans].34,35]

MDCT scans are the preferred comprehensive imaging modality for patients at high risk for PC. This type of CT scan is performed in two phases, an arterial phase and a portal phase, producing hypodense images that improve the detection sensitivity (75–100%) and specificity (70–100%) of the examination [36,37]. The accuracy and sensitivity of CT scans in detecting PC tumors greater than 2 cm in size are high, with a detection accuracy of 73% and sensitivity of 69% for smaller lesions [37].

MRI

MRI has been employed in identifying pancreatic neoplasms when results from ultrasound or CT are equivocal, emphasizing characterizing cystic lesions that cannot be discerned through CT scans. MRI's imaging quality and diagnostic accuracy have been significantly improved with recent advancements in MRI scanners and techniques, resulting in enhanced soft-tissue contrast compared to CT scans [38]. As a result, MRI is now a valuable tool for patients, particularly in detecting small tumors and metastases.

The sensitivity and specificity of MRI studies are in the range of 81–99% and 70–93%, respectively].27,39]

Magnetic resonance cholangiopancreatography (MRCP) is a type of MRI that is particularly useful in detecting narrowing in ductal systems and stones as alternate causes

of biliary or pancreatic ductal dilatation. The sensitivity of MRCP is between 85–87%, while the specificity is between 93–95%. MRCP enables early and successful detection of tumors and analysis of morphological changes within the pancreas [34].

Tissue Biopsy

Tissue biopsy is another invasive diagnostic procedure used in clinical settings. It involves obtaining a small tissue sample from the patient's body, which is then examined in the laboratory, typically through histological analysis, to confirm the condition of the pancreas.

In the context of PC, tissue biopsy involves the procedure of acquiring a sample of pancreatic tissue from a patient intended for subsequent analysis, including histological examination and immunohistochemistry. For diagnostic purposes, various tissue biopsy methodologies are available as alternatives to the conventional open surgery approach. These include laparoscopic procedures, FNA (fine needle aspiration), and FNB(fine needle biopsy) aimed at mitigating the potential of complications, minimizing the postoperative impact, and reducing recovery time.

Laparoscopy, used for diagnostic purposes, involves the insertion of a camera (laparoscope) through small incisions in the abdomen. This approach allows for the localization of the pancreatic tumor, aiding in cancer staging and guiding the resection decision [40]. In contrast to invasive laparoscopy, FNA and FNB are minimally invasive methodologies that entail endoscopic procedures inserted through the oral cavity to the surrounding pancreatic region. The aforementioned EUS-FNA and endoscopic ultrasound fine-needle biopsy (EUS-FNB), utilizing a larger needle, employ an endoscope equipped with an ultrasound probe to visualize the precise location of suspected lesions and to extract biopsy samples or tissue for further examination].26]

Concerning potentially suspicious lesions, histological examination serves as a straightforward approach to analyzing tissue types under a microscope, involving processes such as fixation, sectioning, and staining. Conventional histological staining entails retaining the chemical compounds of the tissue to differentiate various protein types, while immunohistochemistry (IHC) employs antibodies labeled with colored dyes to localize specific proteins within tissues or cells [41].

Biomarker Detection in Bodily Fluids

Conversely, molecular tumor profiling can serve as a cancer diagnosis tool. Still, the current approach of profiling tumors by invasive tumor sampling and histological analysis faces challenges due to the heterogeneous nature of resected tumor tissue samples [42,43]. This limits the quantity and quality of collected samples. Consequently, non-invasive techniques have gained popularity for their convenience in enabling repeated sampling throughout treatment. Although imaging techniques can detect PC, their effectiveness at early stages is limited by the small size of cancer tumors [44]. In contrast, precision medicine relies on a comprehensive understanding of an individual's health status and disease stage and uses omics, such as genomics, transcriptomics,

metabolomics, glycomics, proteomics, and volatolomics, to identify cancerous markers and improve cancer screening, diagnosis, and treatment [45].

Circulating Tumor Cells and Circulating DNA

Circulating cell-free DNA (cfDNA) can be found in the bloodstream from various cells, including hematopoietic cells, healthy cells, apoptotic cells, and circulating tumor cells (CTCs) [46]. In the context of cancer diagnosis, the cfDNA method may not be suitable for clinical decision making due to other factors that can alter cfDNA levels, such as inflammation, exercise, smoking, trauma, and innate chromosomal abnormalities [٤٧]. Within cfDNA, there is a specific subset known as circulating tumor DNA (ctDNA), which is derived from tumor cells. The ctDNA makes up less than 1% of cfDNA. The level of ctDNA released from cancer cells may vary depending on the sensitivity to chemotherapy, ranging from 0.1% to over 90% of all cfDNA Fields [٤٨]. Detecting ctDNA levels indicates 48% of patients with localized cancer and >80% with late-stage pancreatic cancer. The ctDNA can potentially influence metastasis development or cancer gene expression in the body [49].

Volatile Markers

Volatile organic compounds (VOCs) refer to carbon-based molecules in a gaseous state at room temperature due to their high vapor pressure properties. VOCs, as the terminal cell metabolism with poor solubility in blood, traverse the circulatory system and are finally emitted in diverse biological fluids, such as blood, breath, feces, milk, saliva, semen, sweat, and urine [50]. In medical practices, these fluids are frequently used as VOC detection samples due to their easy accessibility and inexhaustibility [51]. However, collecting VOC samples requires specific procedures. For example, blood VOCs are obtained through a standard peripheral venipuncture [52], while breath VOCs are collected using a facemask–airbag system or breath sampler, which filters environmental air from the system].53]

VOCs in the bodily fluids can be used to analyze an individual's metabolic state. Healthy individuals can contain up to 2746 VOCs in their body fluids [54], whereas cancer patients 'VOC profiles may result from the dysregulation of metabolic pathways associated with tumor growth [51].

Method of treatment:

Treatment options and recommendations depend on several factors, including the type and stage of cancer, possible side effects, and the patient's preferences and overall health. When detected at an early stage, pancreatic cancer has a much higher chance of being successfully treated. However, there are also treatments that can help control the disease for patients with later stage pancreatic cancer to help them live longer and more comfortably. The branches of treatment are:

• Surgery.

• Radiation therapy
• Chemotherapy.
• Immunotherapy.
• Physical, emotional, and social effects of cancer
• Dite

Surgery
After a thorough preoperative workup, the surgical approach can be tailored to the location, size, and locally invasive characteristics of the tumor. Curative resection options include pancreaticoduodenectomy, with or without sparing of the pylorus; total pancreatectomy; and distal pancreatectomy. Each procedure is associated with its own set of perioperative complications and risks, and these points should be taken into consideration by the surgical team and discussed with the patient when considering the goal of resection. In qualified high-volume centers, pancreatic surgery (especially distal pancreatectomy, but including pancreaticoduodenectomy) can often be performed laparoscopically.[55] About 20% of people diagnosed with pancreatic cancer are able to have surgery because most pancreatic cancers are found after the disease has already spread. When surgery is a potential treatment option, there are many things to think about before a surgery of this type.

Laparoscopy.
Sometimes, the surgeon may choose to start with a laparoscopy. During a laparoscopy, several small holes are made in the abdomen and a tiny camera is passed into the body while the patient receives anesthesia. Anesthesia is medication to help block the awareness
of pain. During this surgery, the surgeon can find out if the cancer has spread to other parts of the abdomen. If it has, surgery to remove the primary tumor in the pancreas is generally not recommended.

Whipple procedure.
Patients who will most likely benefit from this procedure have a tumor located in the head of the pancreas or the periampullary region. The Whipple procedure is not strictly the surgical approach for pancreatic head tumors. Pancreatic ductal tumors, cholangiocarcinoma (bile duct cancer), and duodenal masses will all require this resection. The operation traditionally involves removal of the pancreatic head, duodenum, gallbladder, and the antrum of the stomach, with surgical drainage of the distal pancreatic duct and biliary system, usually accomplished through anastomosis to the jejunum. The primary reason for removing so much of the intra-abdominal structures is that they all share a common blood supply. Pancreaticoduodenectomy has been shown to have an overall mortality rate of 6.6%.[56] Many forms of morbidity are associated with the operation. One of these is delayed gastric emptying. This occurs in approximately 25% of patients. This condition may require nasogastric decompression

and will lead to a longer hospital stay.[84] Other morbidities include pancreatic anastomotic leak. This can be treated with
adequate drainage. Postoperative abscesses are not uncommon.

Distal pancreatectomy

Essentially, a distal pancreatectomy may be an effective procedure for tumors located in the body and tail of the pancreas. Unfortunately, masses located in this area present later than the periampullary tumors and hence have a higher unresectability rate. The procedure involves isolation of the distal portion of the pancreas containing the tumor, followed by resection of that segment, with oversewing of the distal pancreatic duct. The main complications for distal pancreatectomy involve pancreatic stump leak, hemorrhage, and endocrine insufficiency.[57] Once again, the best treatment for pancreatic leak is adequate drainage.

Total Pancreatectomy

Although this procedure is the least commonly performed and has the highest associated mortality rate (8.3%), it may still be a valuable instrument in the surgical cure of pancreatic cancer. [58] The indication for the use of total pancreatectomy is in cases in which the
tumor involves the neck of the pancreas. This can either be a situation in which the tumor originates from the neck or is growing into the neck. These patients obviously get insulin-dependent diabetes. In some cases, the diabetes can be hard to control. Despite this, the morbidity of a total pancreatectomy is comparable to that of a Whipple procedure. [59]
After surgery, you will need to stay in the hospital. How long you will need to stay in the hospital for will be determined by the type of surgery you've had, but it can range from several days to several weeks or longer. It will also include an at-home rest and recovery plan. At-home rest could be for about a month or longer with full recovery expected to take about 2 months.

Side effects of surgery include weakness, tiredness, and pain for the first few weeks after the procedure. Other side effects caused by the removal of the pancreas sometimes include difficulty digesting food and diabetes from the loss of insulin produced by the pancreas.

Radiation therapy

is the use of high-energy x-rays or other particles to destroy cancer cells. The procedure itself is painless.

There are different ways that radiation therapy can be given:

Traditional radiation therapy. This is also called conventional or standard fraction radiation therapy. It is made up of daily treatments of lower doses of radiation per fraction or day. It is given over 5 to 6 weeks in total and is generally given during the week with weekends off from treatment.

Stereotactic body radiation (SBRT) or cyberknife. These are shorter treatments of higher doses of radiation therapy given over as few as 5 days. This is a newer type of radiation therapy that can provide more localized treatment in fewer treatment sessions.

Proton beam therapy. This is a type of external-beam radiation therapy that uses protons rather than x-rays. At high energy, protons can destroy cancer cells. This type of therapy also lessens the amount of healthy tissue that receives radiation. Proton beam therapy may be given for a standard amount of time or for a shorter time like SBRT.

Radiation therapy may be helpful for reducing the risk of the pancreatic cancer returning or re-growing in the original location. However, there remains much uncertainty as to how much, if at all, it lengthens a person's life.

Possible side effects

Some of the more common side effects of radiation therapy include:

- Skin changes in areas getting radiation, ranging from redness to blistering and peeling
- Nausea and vomiting
- Diarrhea
- Fatigue
- Loss of appetite
- Weight loss

Radiation can also lower blood counts, which can increase the risk of serious infection.

Chemotherapy

is the use of drugs to destroy cancer cells, usually by keeping the cancer cells from growing, dividing, and making more cells. The most active agents for pancreatic cancer have been 5-fluorouracil (5-FU) and gemcitabine. Gemcitabine appears to be slightly more active than 5-FU. Both of those agents are commonly used in combination regimens—for
example, 5-FU plus folinic acid [leucovorin], irinotecan, and oxaliplatin (FOLFIRINOX); and gemcitabine plus capecitabine (GemCap). Objective responses, meaning actual regression of tumor, have been 20% or less. Olaparib, a poly (ADP-ribose) polymerase (PARP) inhibitor, is used for maintenance therapy in pancreatic adenocarcinoma. Olaparib has US Food and Drug Administration (FDA) approval for adults with germline BRCA-mutated metastatic pancreatic adenocarcinoma whose disease has not progressed on at least 16 weeks of a first-line platinum-based chemotherapy regimen.[61,62]

Gemcitabine

frequently quoted trial showed a small, but statistically significant,
improvement in overall survival with gemcitabine versus 5-FU (5.7 vs 4.4 mo).
Additionally, gemcitabine improved the quality of life in approximately 25% of
patients. It is a pyrimidine antimetabolite that nhibits DNA polymerase and

ribonucleotide reductase, which in turn inhibit DNA synthesis.

Fluorouracil (Adrucil)
This is a fluorinated pyrimidine antimetabolite that inhibits thymidylate synthase (TS) and also interferes with ribonucleic acid (RNA) synthesis and function. Fluorouracil has some effect on DNA and is useful in symptom palliation for patients with progressive disease. It is commonly used in patients with gastrointestinal malignancies. Response rates are typically less than 20% in pancreatic cancer.

Erlotinib (Tarceva)
This agent is pharmacologically classified as a human epidermal growth factor receptor type 1/epidermal growth factor receptor (HER1/EGFR) tyrosine kinase inhibitor. EGFR is expressed on the cell surface of normal cells and cancer cells. Erlotinib has been approved by the FDA for use, in combination with gemcitabine, as a first-line treatment for locally advanced, unresectable, or metastatic pancreatic cancer.

Capecitabine (Xeloda)
Capecitabine is a prodrug of fluorouracil that undergoes hydrolysis in liver and tissues to form the active moiety (fluorouracil), inhibiting thymidylate synthetase, which in turn blocks methylation of deoxyuridylic acid to thymidylic acid. This step interferes with DNA, and to a lesser degree with RNA synthesis.

Irinotecan liposomal (Onivyde)
Irinotecan sucrosofate salt in a pegylated liposomal formulation. Irinotecan and its active metabolite SN-38 bind reversibly to the topoisomerase-1 DNA complex and prevent re-ligation of the single-strand breaks, leading to exposure time-dependent double-strand DNA damage and cell death. Irinotecan liposomal is used in combination with fluorouracil and leucovorin for metastatic adenocarcinoma of the pancreas after disease progression following gemcitabine-based therapy.

Oxaliplatin (Eloxatin)
Platinum coordination compound that inhibits DNA synthesis; cross-links and denatures strands of DNA; disrupts DNA function by covalently binding to DNA bases.

And other such as :
- **Leucovorin (Wellcovorin)**
- **Nab-paclitaxel (Abraxane)**
- **Nanoliposomal irinotecan (Onivyde)**

Combination treatments are usually best for people who are able to carry out their usual activities of daily living without help. This is because there are generally more side effects when 2 or more drugs are used together. The choice of which combination to use

varies depending on which is most appropriate for the patient based on their specific diagnosis, stage of disease, treatment history, genetics, side effects, and overall health. Other influencing factors can include the cancer center and the oncologist's experience with the
drugs.

First-line chemotherapy. This is generally the first treatment used for people with either locally advanced or metastatic pancreatic cancer who have not received prior treatment .

The two most common first-line chemotherapy combinations used for pancreatic cancer are
(1) FOLFIRINOX (5-FU, leucovorin, irinotecan, and
oxaliplatin) and
(2) gemcitabine plus nab-paclitaxel.

Side effects of chemotherapy
The side effects of chemotherapy depend on which drugs you receive. In addition, not all patients have the same side effects even when given the same drug. Side effects in general can include poor appetite, nausea, vomiting, diarrhea, gastrointestinal problems, rash, mouth sores, hair loss, and a lack of energy. People receiving chemotherapy are also more likely to have low levels of white blood cells, red blood cells, and platelets, which give them a higher risk of **anemia**, infections, and bruising and bleeding easily.

Immunotherapy
Immunotherapy uses the body's natural defenses to fight cancer by improving your immune system's ability to attack cancer cells. Immune checkpoint inhibitors, which include anti-PD-1 antibodies such as pembrolizumab (Keytruda) and dostarlimab (Jemperli), are an option for treating pancreatic cancers that have high microsatellite instability (MSI-H) or
mismatch repair deficiency (dMMR) . Approximately 1% to 1.5% of pancreatic cancers are associated with high MSI-H. Immunotherapy, combined with chemotherapy, is also being studied as part of emerging clinical trials.

Physical, emotional, and social effects of cancer
Cancer and its treatment cause physical symptoms and side effects, as well as emotional, social, and financial effects. Managing all of these effects is called palliative care or supportive care. It is an important part of your care that is included along with treatments intended to slow, stop, or eliminate the cancer. Palliative care focuses on improving how you feel during treatment by managing symptoms and supporting patients and their families with other, non- medical needs. Any person, regardless of age or type and stage of cancer, may receive this type of care. And it often works best when it is started right

after a cancer diagnosis. People who receive palliative care along with treatment for the cancer often have less severe symptoms, better quality of life, and report that they are more satisfied with treatment.

Supportive care:

• Used in conjunction with active anticancer therapy or as a first line in patients nearing the end of life

• • Pain relief - non-opioid analgesics and opioid analgesics, celiac plexus analysis is performed endoscopically or under CT guidance.

• • Endoscopic interventions to treat biliary or duodenal obstruction resulting from pancreatic cancer

• • Dietary and nutritional support, and management of pancreatic insufficiency

• Behavioral support focusing on coping mechanisms, anxiety, and depression for both patients and their fam[63]

Diet

As with most patients with advanced cancer, patients with pancreatic carcinoma are often anorexic. Pharmacologic stimulation of appetite is usually unsuccessful, but it may be tried.

Patients may have some degree of malabsorption secondary to exocrine pancreatic insufficiency caused by the cancer obstructing the pancreatic duct. Patients with malabsorption diarrhea and weight loss may benefit from pancreatic enzyme supplementation. Their diarrhea may also be improved by avoidance of high-fat or high-protein diets

Chapter two

Patients and Methods

Patients and Methods:

The study design was a retrospective hospital-based record study in which records of 40 pancreatic cancer patients registered, evaluated, and treated at Iraq cancer control center from November 2024 through March 2024 were studied. This study included an estimation for the levels of some biochemical parameters in the serum of those pancreatic cancer patients, by collecting (40) blood samples from patients their ages ranged (30-90) years compared with (50) blood samples of healthy persons as control group. The parameters included Super oxide dismutase, Amylase, liver function test, kidney function test, lipid profile, carbohydrate antigen 19-9. A questionnaire is used to gather information about the patient and including name, home address, age, sex, height, weight, whether the patient is a smoker, whether he has chronic diseases, history of chronic disease and history was taken, full physical examination was performed. Also, a questionnaire is used to gather information about the doctor's health awareness of this cancer. In all operated-on patients, biopsy was taken and submitted to histopathological examination by expert pathologist. CT scan, MRI of the abdomen was not done because, it was not available at time of the study in our hospitals.

Statistical Analysis:

The results were expressed as the mean ± standard deviation or as simple percentages as appropriate for all other variables with normal distribution, data were presented as mean [standard deviation (SD)]. Otherwise, the median values were presented for variables which were not normally distributed. Mean and/or median of the study variables between groups were compared using analysis of variance (ANOVA), Kruskal-Wallis, Wilcoxon test (when appropriate), and Post hoc tests. Chi-square was used for comparing the frequencies. The differences were considered significant at p values of less than 0.05. Statistical analysis was conducted using the SPSS software (version 15) (SPSS Inc., Chicago, USA).

Chapter Three

Result and Discusion

Results:

Forty with pancreatic carcinoma were studied, 30(77.78%) patients were males, and 10(22.22%) patients were females with males to female's ratio of 3:1. Their age range from 30 to 90 years with an average of 58.73. Most 15(37.5%) patients were in the age group 50-70 years, only 10(25%) patients were in the age group 70-90. An interesting observation that 5 patients (12.5%) were under 50 years (Table 1) and (Table 2).

Table 1: Shows the number of people with gender by pancreatic cancer.

gender	Frequency	Percent
male	30	77.78
female	10	22.22
total	40	100

Table 2: Shows that the age groups affected by pancreatic cancer.

gender	Frequency	Percent
30-50	5	12.5
50-70	15	37.5
70-90	10	25
Total	40	100

The commonest risk factor was smoking occurred in 20(50%) patients, this was followed by diabetes mellitus occurred in 12(2.5%) patients (Table 3). Jaundice was the commonest presenting symptom 32(57.5%) patients, followed by weight loss 10 (25%) patients and abdominal pain 10 (25%) patients (Table 3).

Table 3: The clinical features of patients studied.

Risk factors	No. (%)	Presenting symptoms	No. (%)
Smokers	20(50)	Jandice	23(57.5)
Diabetes mellitus	12(30)	Weight loss	10(25)
Alcoholic	1(2.5)	Abdominal pain	10(25)
Other factors	7(17.5)	Vomiting	1(2.5)
		Back pain	2(5)

***Patients may have more than one presenting symptom or physical sign.**

This study showed that ultrasonic examination was good tool for the diagnosis and assessment of these patients, it was either able to detect the tumors (26 patients in the head of pancreas and 6 patients in the body), or its effect on billiary tree (dilatation of intra and extrahepatic billiary tree in 30 patients) or evidence of liver metastasis (9 patients). (Table 4).

Table 4: The ultrasonic findings.

U/S findings	No.	%
Dilatation of intra and extra hepatic biliary tree	30	75
Mass at the head of pancreas	26	65
Mass at the body of pancreas	6	15
Liver secondary	5	12.5

***Patients may have more than one finding.**

Most cases were very advanced at time of diagnosis. Out of 40 patients only 35 (79.54) patients were operated on. Only in 25 (71.4%) patient, curative Whipple procedure was possible, while in 10 patients only billiary bypass surgery were done and in one patient only biopsy was taken from the tumor (Table 4 and 6). Tumor of the body of pancreas was very much infrequent than the head and was detected in 6 (15%) patients (Table 5). Adenocarcinoma was the commonest histopathological type observed in 90% of patients. Poorly differentiated carcinoma was seen in 10 % of operated patients. No endocrine tumors were reported in this study 10 patients could not be followed-up, non-of the remainder 30(75%) patients survived for one year.

Table 5: The site of the tumours and the evidence of liver or local metastasis in the studied patients.

The operative finding*	No.	%
Tumour of the head	30	75
Tumour of body	6	15
Liver secondary	6	15
Evidence of LN or local metastasis	12	30

***Patient may have more than one finding**

Table 6: The surgical treatment and type of surgery that was done in studied patients.

The surgical treatment	No.	%
Surgery was done	30	75
Not fit for general anaesthesia	5	12.5
Refuse surgery	5	12.5
Type of surgery		% from operable patient
Whipple procedure	25	71.4
By pass procedures	10	28.6
Biopsy	5	14.3

Results of this study indicated a significant decrease in the activity of Amylase and Super oxide dismutase patients in comparison with the control group. There was a significant increase in liver function test, kidney function test, carbohydrate antigen 19-9, Total lipid in patients in comparison with the control (Table 7).

Table 7: The comparison of serum biochemical parameters between Patients and Control group($p \leq 0.05$) Parameters Mean ± Standard error Patients (40) and Control (50)

Parameters	Mean ± Standard error	
	Patients (40)	Control (50)
Super oxide dismutase (µmol/L)	0.031±0.016	0.096±0.007
Amylase (U/L)	52.739±10.344	70.318±4.28
Alkaline phosphatease(U/L)	302.2±40.78	44.89 ±3.5
Bilirubine (µmol/L)	20.1±5.3	6.1±1.835
Total Lipid (mg/ml	1370.4±26.9	647.14±20.6
Urea(mg/dl)	11	24±20.6
Creatinine	0.5	0.7±10.6
Ca 19.9 (U/ml)	23.5±1.73	8.5±0.75

Discussion:

Carcinoma of pancreas occurred more frequent in males than females with males to females ratio of 3:1 in this study, this was consistent with other studies 3,6,7 . Most patients were in the age group range of 50-70 and this was in contrast with other study done in western countries (8) in which this maximally occurred above 75 years, this may be explained by short life expectancy of Iraqi people and high incidence of the disease in younger age group 3 . An interesting observation was that 5 (12.5%) patients were under the age of 50, this was consistent with Alkafaji et al 3 who reported 7.2 % under 40, and they report carcinoma of pancreas in 26 years old patient Smoking was the commonest risk factor observed in 43.18% of the patients, this was consistent with other studies 9,10 . Smoking was the commonest risk factor observed, this was consistent with other studies (9,10). Fuchs et al, administer that among current smokers, the relative risk of pancreatic cancer, in a large prospective study, was 2.5. The risk fell by 48 percent by two years after discontinuing smoking, and eventually fell to the level of nonsmokers 9 . Silverman et al and Fuchsia et al have estimated that cessation of smoking could eliminate approximately 25 % of pancreatic cancer deaths in the United State 9, 10 . Diabetes mellitus was the second commonest risk factor occurred in 9(24%) patients, in this it was consistent with other studies 10, 11 . A case-control study found an odd ratio for pancreatic cancer of 1.5 to 1.6 compared to non-diabetics among patients with diabetes for at least 10 years 10 . The risk was similar in type 1 and type 2 diabetics. Other study found that glucose intolerance without overt diabetes was also a significant risk factor, suggesting that factors associated with abnormal glucose metabolism may have a significant role in the etiology of pancreatic cancer 11 . Obstructive Jaundice, was the commonest presenting feature occurred in 72% of patients, this was consistent with other studies 3, 12 . This can be explained by the fact that carcinoma of the head of pancreas was the commonest type of pancreatic cancer in this study Vs patients had cancer of the body of pancreas, these tumors usually presented with obstructive jaundice because they compress the billiary drainage earlier, than that of the body of the pancreas which usually presented with abdominal pain and weight loss and this was in consistent with other studies12 . Abdominal mass was detected in 22.2% of the patients, this was consistent with other studies 2,3 . The ultrasonic examination was sensitive tool in detecting the tumors or it's complications in this study, this was consistent with other studies 2,13,14 . Maringhini and Karlosn reported sensitivity and specificity of US in diagnosing pancreatic cancer is 75 to 89 and 90 to 99 percent, respectively; however, these numbers are dependent upon the expertise of the ultrasonographers, the presence or absence of bile duct obstruction, and the extent of the tumor 13,14 . CT scan has a better sensitivity than and similar specificity to ultrasonic examination for the detection of pancreatic cancer 16 It may be particularly useful in-patients who are not jaundiced and in those in whom intestinal gas interferes with ultrasound14 . Only 25 patient was fit for curative Whipple procedure, which suggest that most cases were advanced at time of diagnosis. Regin et al,

administered that only 5% to 15% of patients with pancreatic adenocarcinoma are candidates for a potentially curative resection 16. This explained why patients with Pancreatic cancer continues to carry a poor overall prognosis, because the majority of patients have advanced disease at the time of presentation17 . Even with curative procedure in especial units, a 5-year survival rate was reported to be between 10 and 24% 18 . Results of this study indicated a significant decrease in the activity of Amylase and Super oxide dismutase patients in comparison with the control group. There was a significant increase in liver function test, kidney function test, carbohydrate antigen 19-9, Total lipid in patients in comparison with the control

Chapter four

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