

Literature Review

Factors associated with late presentation of cancer: a limited literature review

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Abstract

According to the World Health Organization (WHO 2006), cancer is one of the leading causes of death worldwide. Deaths from cancer are projected to continue rising, with an estimated 9 million people dying from cancer in 2015 and 11.4 million dying in 2030 (WHO 2006). Delayed presentation or late diagnosis of cancer is associated with low survival. The aim of this review is to identify factors associated with delayed presentation of cancer that were reported by previous studies. Published studies which identified the most common factors attributed to the late presentation of cancer were reviewed. Publications were identified using MEDLINE (Medical Literature Analysis and Retrieval System Online), the Cochrane Library, CINAHL (Cumulative Index to Nursing and Allied Health Literature) and EMBASE (Excerpta Medica Database) databases. A Critical Appraisal Skills Programme (CASP) was used to assess the methodological quality of the studies. A total of 24 studies met the inclusion criteria. A data extraction sheet was used to systematically record relevant factors. Twenty-four studies met the inclusion criteria which identified factors associated with patients' delay including patients' knowledge, stress and fear, and nature of the disease. Other factors were attributed to health providers such as general practitioner (GP) experience, referral delay, and a younger age group being considered as low risk, so symptoms were missed.

Keywords

Cancer; delay; diagnosis; late presentation; patients; time factor; treatment

INTRODUCTION AND METHODS

The following electronic bibliographic databases were searched: OVID MEDLINE (Medical Literature Analysis and Retrieval System Online), 1966 to March 2008; OVID EMBASE (Excerpta Medica Database), 1980 to June 2008; Cochrane library; ASSIA (Applied Social Sciences Index and Abstracts); CINAHL (Cumulative Index to Nursing and Allied Health Literature); and DARE (Database of

Actuarial Research Enquiry). Boolean method was used, and 21 articles were selected as relevant to the research question. Using 'find cited article' and 'find similar article', 12 additional articles were identified and selected for the review (total = 33). The final number of articles used for this review was 24 after excluding 9 articles which did not match the inclusion criteria.

The studies included in this review were all qualitative studies (particularly focus groups and interviews). All qualitative studies that focused on factors related to delay in presentation

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and investigated all types of cancers were included. The review included studies that recruited patients over 20 years of age. Studies that included children and young adults were excluded for two reasons. Firstly, children are dependent on their parents to make decision to seek help. Secondly, cancer in young adults is not common, and this may affect physicians' decision during diagnosis. Studies were included that reported findings which were believed to contribute to late presentation, and delayed diagnosis and treatment of cancer and also those that investigated delays in referrals and the effect of delay on survival.

All studies written in English were assessed using a Critical Appraisal Skills Programme (CASP). Studies written in other languages were not included due to time and translation constraints. The CASP is a program to assess the methodological quality of the study included under these criteria: (1) clear statement of the aims; (2) appropriate methodology including the right participants and the research design; (3) addresses the aim of the research; (4) setting for data collection was justified; (5) ethical issues were taken into consideration; (6) data analysis is sufficiently rigorous; (7) clear statement of findings; (8) the research is valuable.

Using a data extraction sheet, the data extracted from these studies were categorised under two main categories: firstly, factors associated with patients' delay, and secondly, factors associated with health system delay. The designs of the studies reviewed vary between inductive designs, where the generation of theory for the aim and meaning of experience was explored, and deductive designs where variables were examined.

The definition of 'patient delay' applied here is that used by de Nooijer et al.¹ who defined patient delay as the interval between the day someone first becomes aware of an unexplained symptom and the day they seek medical consultation. The most common factors associated with late presentation of patients with cancer identified in this review are discussed below.

Knowledge and education

A considerable amount of literature has been published on patients' knowledge and education as a determinant factor for delay in presenting their symptoms to a health professional. Patients with low education and less knowledge about cancer were found to have delayed reporting their disease.² Low education and less knowledge about cancer have also been reported in a study conducted in the Netherlands³ where patients with head and neck cancers who delayed reporting their disease were found to be less educated. In this study, a median delay of 7 weeks from the time of consulting a dentist or a general practitioner (GP) until patients were referred to a surgeon or an otolaryngologist. Delays were found to be associated with the cognitive interpretation of the symptoms. For example, patients who suspected cancer, and had knowledge of head and neck cancer, were more likely to return to the GP or the dentist after the first consultation if symptoms persisted. The study, however, did not mention how long patients waited from the time of first noticing their symptoms until the time they consulted their doctors. It is also not clear why dentists or GPs waited 7 weeks to refer patients to a surgeon.

Education and socio-demographic variables were also found to be predictive of a significant amount of variance in patient delay by Llewellyn et al.⁴ who investigated factors associated with delay in presentation among younger patients with oral cancer. They found that low educational status was the most consistent factors associated with delay in patients. This is consistent with the findings from Tromp et al.³ who stressed a relationship between patient delay and knowledge of symptoms. An Australian study, utilising random telephone interviews with patients with colorectal cancer,⁵ reported that 23% of their samples ($n = 1,332$) who experienced bowel blood did not seek medical advice at all. Reasons for not seeking advice included the following: (1) thought it was not serious; (2) tests would be embarrassing; (3) may clear by itself.

de Nooijer et al.¹ utilised Andersen's model of patient delay⁶ referred to above to investigate factors influencing the processes of detecting

cancer symptoms and consulting a GP. Andersen's model describes the pre-diagnostic period comprising six stages in which delay can occur. This model divides the details of delay into categories (appraisal delay, illness delay, behavioural delay, scheduling delay, and treatment delay). de Nooijer et al.'s study¹ involved semi-structured interviews with 23 patients. Six patients had breast cancer; five patients had testicular cancer; six patients had colon cancer, and six patients had melanoma. Knowledge was regarded as a stimulating factor in recognising the illness since it is a pre-requisite for interpreting the illness. This finding was similar to those of a study conducted in Germany which examined provider delay among patients with breast cancer.⁷

Stress and fear

Burgess et al.⁸ investigated women's delay presenting with breast cancer and reported that some women had past experience of a member of the family who had a painful death and they feared the same experience. One patient refused the referral until terminally ill as reported in a study investigating the effect of delays in primary care referral of women with ovarian cancer.⁹ Fear during the first medical consultation was reported as a causative factor for delay. Some patients reported fear of being told they had cancer, and one patient said she cancelled her appointment.¹ Fear of being diagnosed with cancer and its social consequences were found as a barrier to mammography.¹⁰

Llewellyn et al.⁴ found that with patients who reported stress in the period prior to diagnosis, delay was found to be seven times higher. Furthermore, that feeling unworthy of treatment was a factor for not seeking help.¹¹ Semi-structured interviews may be an important tool here as they may give the researcher the opportunity to explore the processes of fear as a barrier to consulting a doctor or a member of the family. Fear, however, could also be a stimulating factor to seek help. Some people, when they experience or notice a minor change in their health, may start worrying about having a serious disease and then look for more than one medical consultation

or opinion to make sure there was nothing wrong with them. This is an area where further investigations are needed.

Nature of the disease

It has been reported that signs and symptoms of the disease have an influence on late presentation.^{8,12} The nature of the disease and the presence of an obvious lump, bleeding, or unusual pain may prompt the patient to consult a GP. On the other hand, absence of pain and obvious symptoms may delay patients seeking help.¹¹ A possible explanation for this might be that pain and bleeding may not be tolerated, and the patient has to see a doctor for relief of these symptoms.

This pattern of help-seeking behaviour may possibly be applied to other cancer types; some diseases such as oral cancer appear as a painless ulcer in the mouth, and the patient may think it could be a benign routine ulcer which may clear of its own accord. This pattern of behaviour has also been reported in other studies investigating delays in head and neck cancers where 24% of patients did not consider the symptoms worrying.¹³ This study described how almost two thirds of 51 patients who had oral cancer consulted their doctors within 2 months where the other third did not. Lung cancer was considered as one of the diseases where late presentation occurs due to the nature of symptoms.¹¹ The authors argued that patients live with symptoms, such as a cough, for a long period until they cough blood (haemoptysis) which then prompts the patient to see a GP. Corner et al.¹¹ did not intend to investigate the factors associated with late presentation of lung cancer, rather, they were exploring the symptoms which prompted patients with lung cancer to visit a doctor. However, the point made here, that some diseases such as lung cancer (which is common) may not be reported until serious symptoms develop, is an important one. However, although Corner et al. attributed the delay to patients' misinterpretation of the seriousness of their symptoms, there is no information in the study about when patients were actually diagnosed and then treated following their first visit to the doctor.

Mor et al.'s¹² study combined investigation into three common types of cancers. They investigated pre-diagnostic symptom recognition and help-seeking among patients with breast, lung and colorectal cancers. Patients were asked questions relating to their recognition of symptoms using semi-structured interviews. The majority of patients reported noticing the symptoms prior to diagnosis (79.7%). Patients with more advanced disease were more likely to recognise symptoms than patients with a local disease.

Findings from another study¹ revealed that the reaction to the detection of symptoms seemed to be associated with the nature of the disease, as some symptoms were regarded as normal, such as cough for those with lung cancer. These findings are similar to those of Corner et al.¹¹ Also, Mor et al.¹⁴ found that patients with lung cancer are more likely to delay than those with breast cancer, unlike patients with colorectal cancer with rectal bleeding and whose symptoms motivate them to seek help. In contrast, ovarian cancer is rare and difficult to diagnose.^{9,12} The nature of the symptoms is general, such as abdominal pain, and it was reported that some patients were referred to a gastrointestinal specialist before they were referred to a gynaecologist or oncologist.¹²

In summary, the nature of the disease plays a significant role in late presentation as patients may think some symptoms are normal and then do not seek help until the disease progresses, and GPs may interpret and attribute some symptoms to other disorders. In order not to be misled by the symptomatology of a disease when conducting research investigating factors associated with delay among patients with cancer, in general, it is important to recognise that some cancers are much harder to interpret and diagnose than others.

Socioeconomic status

Socioeconomic status plays a role in patterns of late presentation as patients who have to pay for cancer consultation and treatment might have to stop seeing a physician because of shortage of funds^{15,16} and transportation difficulties.^{15–18} There is considerable debate

about this as Tromp et al.,³ in a more recent study, concluded that there was no significant association between delay and socioeconomic status in the patients with head and neck cancers that he interviewed. In some countries, however, a doctor's consultation and treatment is not free if the patient has no health insurance provided by the government. Some other countries, such as the UK, the investigation and treatment of cancer is free at the point of receipt, but late presentation of symptoms still occurs.

Coping style

Patients who were more likely to seek support as a coping style showed less delay seeking medical care.³ de Nooijer et al.¹ revealed that patients who had not consulted relatives or friends, or who ignored other people's advice, seemed to have postponed the decision to seek medical help. Some patients found discussing some symptoms with others embarrassing, especially those with rectal cancer.¹ Perception of competing priorities has been reported⁸ as an explanation for patients' delay as some patients felt too busy with other priorities, such as families and holidays, which seems to reflect the tendency of some people to place the needs of others above their own.

Factors associated with providers delay

Providers delay was defined as the time period beginning from a patient seeking an evaluation of self-discovered symptoms ending at the initiation of treatment.¹⁷ Providers delay is the delay caused by health providers, such as GPs, specialists, or the health system itself. Specialists' referrals, waiting lists, and poor coordination were reported in a Spanish study as some of the factors associated with provider's delay.¹⁹ The most common findings reported in the literature reviewed attributing the delay to health providers are as follows: GP experience in recognising the symptoms, referral delay and younger patients being regarded as low risk for many cancers resulting in misdiagnosis.

GP experience

GPs did not always investigate malignancy as a possible cause of all the reported symptoms.¹²

Evans et al. interviewed women with ovarian cancer about how they reported their symptoms. For example, a post-menopausal woman developed a 'period-type pain' and her GP found nothing wrong with her. She was advised to return if the pain persisted. Another woman mentioned that her GP attributed her lower abdominal pain to a cyst that had burst. Some GPs do not treat some signs and symptoms as seriously as others, or may understandably attribute the symptoms to other causes. It could also be a combination of the nature of ovarian cancer, which is rare and difficult to diagnose,^{9,12} and the experience of the GP will influence late diagnosis. It also appears that if patients were given treatment, such as antibiotics or pain killers, for a 'non-cancer' cause, patients may not always return to see the doctor.¹² The medication given may reduce the pain and therefore convince the patient that nothing was wrong. GPs have been criticised before by the UK government for not identifying patients with suspected cancer.²⁰ Unfortunately, Evans et al.¹² were unable to interview GPs, and they considered this as a weakness of their study. It was not clear why they were unable to interview GPs; however, they stressed that the factors attributed to providers' delay need further investigation.

One further critical finding reported by Tromp et al.³ was that only 6% of patients who were not referred or followed up mentioned that they returned to the GP (or dentist) because they were advised to return if symptoms persisted. This means 94% of patients, who were not referred or followed up, were not advised to return to be seen again if the symptoms persisted, although they had potential warning signs for something more serious. Some patients had decided not to seek for help because they thought a GP could not do anything about their complaints and because of the "gate-keeping" function of GP services.¹¹ This function of GPs was described by some patients as 'advocate', 'gatekeeper' or 'the one who controls your entry to the system'.¹⁸ This is clearly an important factor in the possible delay of patients reporting their symptoms to their GP and one that requires further investigation.

Referral delay

One of the problems that may face the GP in primary care centres is lack of diagnostic resources, such as ultrasound and CT (computed tomography) scanners, which may only be available in hospitals. The GP has to refer the patient with suspected symptoms to a specialist who will deal with the case and send a report back to the GP. This may take weeks, and patients may have to be on a waiting list unless the referral is urgent.¹² Like patients who reported a concern with bothering their GP for something not serious,⁸ the GP may have a concern with urgently referring a patient unnecessarily.

Other factors related to providers' delay in diagnosing colorectal cancer was found in a study conducted in the UK²² and included the following: false-negative reporting of barium studies, inaccurate tumour biopsy and inappropriate delay in definitive investigation.

Younger age regarded as low risk

Younger age and presentation with a breast cancer symptom, other than a lump, were strong risk factors for delays by providers.¹² Other studies have also reported that the reason for longer waiting times for younger females with breast cancer was the lower suspicion of cancer.¹⁹ These findings have been confirmed in a study by Miedema²⁰ who investigated young adults' experience with cancer (age between 20 and 35). In this study, which was conducted in a rural area in Canada, six men and nine women were interviewed. They reported that physicians were reluctant to make a diagnosis of cancer because of the patient's relative youth. One 29-year-old man, who had died shortly after the interview, took almost a year to have a final diagnosis of colorectal cancer.

In Facione's literature review,¹⁷ a study in Singapore reported that women under 35 experienced increased provider delay due to expectation of benign disease. Facione reported further that some studies found that 'poor advice' was given to patients. Poor advice was defined as misdiagnosis or false reassurance that the lesion was benign.

Youth was not found to be a factor related to late presentation in Germany when Arndt examined provider delay among patients with breast cancer.⁷ They conducted face-to-face interviews with women newly diagnosed with breast cancer. The questions were about the process of diagnosis, date of first consultation, ultrasound examination and mammography. Forty-six women out of three-hundred and eighty interviewed reported that it took over 14 days after the first consultation before a mammography or biopsy was performed. 11% of patients started their treatment in the third month, 16% in the second month, and 73% within the first month of first consultation. Although there was no explanation for those 11% who waited until the third month, employment status, family history of breast cancer, education, type of symptoms and mode of detection were identified as statistically significant determinants of provider delay. In this study, youth did not emerge as a strong factor for provider delay which contradicts the findings of Miedema²¹ and Facinoe.¹⁷

CONCLUSIONS

Most studies reported here were disease-specific, focusing upon a single disease, such as breast cancer, oral cancer or lung cancer. Therefore, the results obtained cannot be generalised to other types of cancer. In these single-disease studies, the factors that were found to have a role in the late presentation of cancers are more specific to the characteristics and the nature of that disease. Only a few studies^{1,3,14} used wider boundaries and combined more than one disease in one study. None of these studies aimed to explore the factors associated with the late presentation by gathering data from more than one source, such as patients and health professionals, in order to understand the problem from different perspectives.

Most papers reviewed also focused on specific population groups. For example, studies that focussed on breast cancer or ovarian cancer, the population is always women. However, few studies combined diseases where men and women could be recruited. Other studies

focussed on the process of referrals and protocols that should be followed to avoid delay and speed up referral process. Most of these studies were conducted in some modern countries where health awareness and health systems are believed to be superior to those in developing countries. The study conducted by Baumann¹⁶ about breast cancer and care seeking in Vietnam highlighted the weakness of health system in Vietnam where the government spends only \$0.60 per capita compared to \$3,299 per capita in the United States.

There are gaps in the literature specifically in research conducted in developing countries. It was also evident that health providers' delay was under researched and requires further investigation.^{2,3,12,17} What is evident though is that qualitative research has begun to provide insights into various key factors associated with delay in presentation and treatment of various types of cancers for a range of different patient groups. Further research is now needed to tease out similarities and differences across and between different forms of cancers and different patient groups in order to provide a more complete picture of how delays can occur and help ensure the prevention of many needless deaths in the future.

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