Guía de repaso de conocimientos básicos de metodología de la investigación

Temario

1. Validez de una prueba diagnóstica
2. Asociación y causalidad
3. Utilidad de una medida terapéutica
4. Curso clínico o pronóstico
5. Calidad de la atención
6. Evaluación socioeconómica

2. Asociación y causalidad

Objetivo:

- Repasar los criterios metodológicos mínimos requeridos en el diseño de un estudio de etiología o causalidad, para considerar los resultados válidos y reproducibles.
- Repasar los parámetros más comúnmente utilizados para medir aspectos relacionados con etiología o causalidad de las enfermedades.
- Aplicar los criterios y parámetros revisados en un ejemplo de la literatura médica.

Lecturas:

- Department of clinical epidemiology and biostatistics, McMaster University Health Science Center. How to read clinical journals. IV. To determine etiology or causation. *Can Med Assoc J* 1981; 124: 985-990.
- Ramirez Villalobos D, Hernandez Garduno E, Salinas A, Gonzalez D, Walker D, Rojo Herrera G, Hernandez Prado E. Early hospital discharge and early puerperal complications. *Salud Pública Mex* 2009; 51: 212-218.

Ejercicios:

En el artículo sobre etiología de las complicaciones puerperales tempranas en mujeres atendidas en un hospital general, valore si se cumple con los criterios metodológicos recomendados.

Criterio metodológico	**Valoración**
1. Identifique el diseño utilizado.	
2. Comente sobre la fortaleza de este diseño para establecer causalidad.	
3. ¿Existe evidencia experimental en humanos? Si existe evidencia explique en qué consiste.	☐ Si ☐ No ¿Por qué?

Criterio metodológico	**Valoración**
4. ¿Es fuerte la asociación encontrada? Si es fuerte, ¿en qué fundamenta la fortaleza?	☐ Si ☐ No ¿Por qué?
5. ¿Es la asociación consistente de estudio a estudio? ¿Con base a qué considera que existe consistencia?	☐ Si ☐ No ¿Por qué?
6. ¿La relación temporal entre variables es correcta en este estudio?	☐ Si ☐ No ¿Por qué?
7. ¿Qué entiende por relación temporal correcta?	
8. ¿Existe gradiente dosis respuesta en este estudio?	☐ Si ☐ No ¿Por qué?

Criterio metodológico	**Valoración**
9. ¿Qué significa gradiente dosis respuesta en causalidad?	
10. ¿En el estudio analizado la asociación encontrada tiene sentido epidemiológico?	☐ Si ☐ No
	¿Por qué?
11. ¿Qué significa asociación causal con sentido epidemiológico?	
12. ¿La asociación encontrada en el estudio tiene sentido biológico?	☐ Si ☐ No
	¿Por qué?
13. ¿Qué significa asociación causal con sentido biológico?	
14. ¿La asociación encontrada en el estudio es específica?	☐ Si ☐ No
	¿Por qué?

Criterio metodológico	**Valoración**
15. ¿Cómo define asociación específica?	
16. ¿La asociación encontrada en el estudio es análoga a la observada en otra relación causal?	☐ Si ☐ No ¿Por qué?
17. Defina qué entiende por analogía en causalidad.	

How to read clinical journals: IV. To determine etiology or causation

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This is the fourth in the current consecutive series of Clinical Epidemiology Rounds devoted to efficient strategies and tactics for reading clinical journals. The first four guides for reading a clinical journal apply to any article (consider the title, the authors, the summary and the site) and appear in Fig. 1. The fifth guide depends on why the article is being read; the reason that will be considered in this round is to learn more about the etiology and causation of human illness.

Perusal of a grab sample of issues from volume 121 of the Journal reveals that its clinical readers are faced with claims about the etiology and causation of human illness every time they read. For example, they are warned about dietary fibre and colon cancer;[1] cimetidine is implicated as a cause for diminished libido;[2] it is proposed that cigarette smoking has an effect on the risk of occupational lung cancer;[3] heavy tea consumption is blamed for iron deficiency;[4] they learn about drugs that cause dependence;[5] viral encephalitis is proposed as a cause of Huntington's chorea;[6] they are told that malfunctioning brown fat may be a cause of obesity;[7] *Campylobacter* is implicated in the etiology of ileocolitis;[8] they are asked to reconsider whether colour-blindness in auto drivers causes traffic accidents;[9] and, finally, the roles of cold snaps and snow-shovelling as causes of sudden death are debated.[10]

These 10 "cases in causation" have important implications for both private and public practitioners because some powerful recommendations are made: we should try to change our patients' eating habits, have second thoughts about prescribing some specific drugs, discourage tea-drinking in certain native groups, consider (or reconsider) stopping colour-blind people from driving, and stop lots of patients from shovelling snow.

When we add to the foregoing the

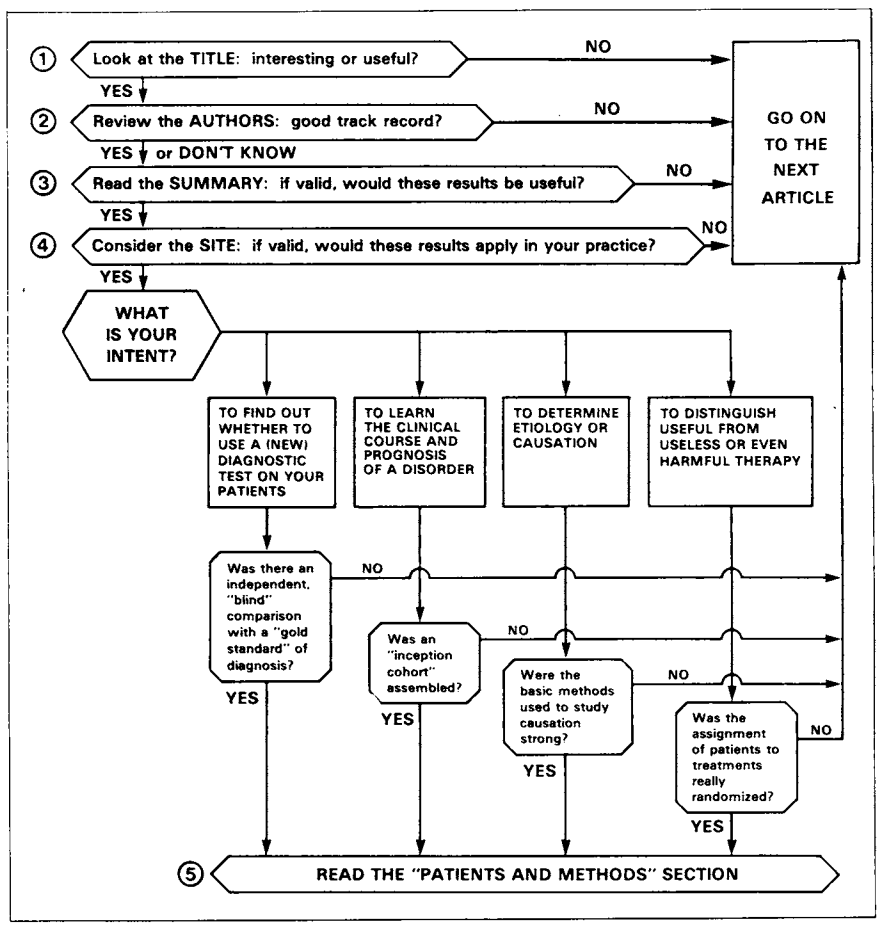

FIG. 1—The first steps in how to read articles in a clinical journal.

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bevy of claims for causation that our patients, to their distress, come upon in the lay press and on television, it becomes clear that clinicians are forced to make judgements and to give advice about causation all the time.

To help meet these demands for instant sagacity we have brought together some "applied principles of common sense" that should help the busy clinician assess an article that claims to show causation. They are distilled from the work of a number of methodologists, most notably Austin Bradford Hill.[11]

The application of these common-sense principles involves two steps. First, readers should scan the Methods section of the article to see whether the basic methods used were strong or weak. Second, they should then apply a set of "diagnostic tests" for causation to the remainder of the article.

Step one: Deciding whether the basic methods used were strong or weak

Sometimes you can identify the basic method used in a study from its title; other times you must examine its abstract or Methods section. Thus, step one can be accomplished quickly, without having to read the Introduction or Discussion. This step is summarized in Table I.

Suppose we really wanted to find out whether snow-shovelling was a cause for heart attack in middle-aged (your age plus 5 years) men. What would be the most powerful sort of study we could find in the clinical literature?

Most of you, we hope, would start by looking for a true experiment in humans — a study in which middle-aged men were randomly allocated (by a system analogous to tossing a coin) to habitually shovel or not shovel snow each winter,* and were then followed to see how many in each group died suddenly. Evidence from such a *randomized trial* is the soundest evidence we can ever obtain about causation (whether it concerns etiology, therapeutics or any other causal issue), and the reasons for this, if not already clear, will become apparent as we proceed. The basic architecture of the randomized trial is shown in Table II.

Although the true experiment (randomized trial) gives us the most accurate (or valid) answer to a question of causation, and therefore represents the strongest method, we will not find it very often in our clinical reading. In many cases (including the present example) it is not feasible to do a randomized trial to determine etiology, and in some it is downright unethical. For example, who would ever consider carrying out a true experiment that would deliberately cause viral encephalitis in a random half of a group of individuals to see whether they were rendered more likely to develop Huntington's chorea?[6]

Thus, we are much more likely to encounter the following subexperimental studies of the risk of heart attack from snow-shovelling. For example, the next most powerful study method, the *cohort study*, would identify two groups (or cohorts) of middle-aged men, one cohort that did and the other that did not shovel snow each winter. The investigators would then follow these two cohorts, counting the heart attacks that occurred in each. In this case the direction of inquiry is forward in time, as depicted in Table III. If the heart attack rate was higher in the cohort that shovelled snow, this would constitute reasonably strong evidence that snow-shovelling precipitated heart attacks. However, the strength of such a cohort analytic study is not as great as that of a randomized trial; the reason for this difference in strength is apparent if we consider the middle-aged man with

Table I—Step one: Deciding whether the basic methods used were strong or weak

Strength	Method
Strongest	Randomized clinical trial
	Cohort study
	Case–control study
Weakest	Case series

Table II—Basic structure of a randomized trial

	Outcome (heart attack)	
	Yes	No
Exposed (shovelled snow)	a	b
Not exposed (did not shovel snow)	c	d

(R)

Direction of inquiry →

Table III—Basic structure of a cohort study

	Outcome (heart attack)	
	Yes	No
Exposed*	a	b
Not exposed*	c	d

(?)

Direction of inquiry →

*Definitions as in Table II.

*Those who balk at the feasibility of this approach should recognize that the point at issue here is validity, not feasibility. On the other hand, the authors could have provided the controls with snow blowers!

angina pectoris. First, is he more likely than his angina-free neighbour to avoid snow-shovelling or other activities that precipitate angina? Yes. Second, is he at higher risk than his neighbour of heart attack? Yes again. Thus, the cohort analytic study could provide a distorted answer to the causal question if men at high risk of heart attack for extraneous reasons* were not equally distributed between the cohorts of those who did and did not shovel snow. We see, then, that we must view a subexperimental study such as the cohort analytic study with some caution and suspicion.

A second type of subexperimental study deserves even greater caution in interpretation — the *case–control study*. In a case–control study the investigator gathers "cases" of men who have suffered a heart attack and a "control" series of men who have not had a heart attack. Both groups of men are then questioned about whether they regularly shovel snow each winter. If those who had heart attacks were more likely to regularly shovel snow, this would constitute some evidence, though not very strong, that snow-shovelling might cause, or at least precipitate, heart attack. Thus, in this case the direction of inquiry is backwards in time, as shown in Table IV.

*You may come upon the term *confounder* in your reading, and that's what angina is in this example. First, it is extraneous to the question posed (What are the effects of snow-shovelling?); second, it is a determinant of outcome (heart attack); and, finally, it is unequally distributed between the cohorts of exposed and nonexposed persons.

Why is the case–control analytic study low on the scale of strength? Because it is so very liable to bias. The case–control study is susceptible not only to bias from the angina patient we noted in the cohort study, but also to several other sorts of bias.[12] For example, if snow-shovelling precipitated not only heart attack but also sudden death, many victims would not survive long enough even to be included in a case–control study, much less to be interviewed. As a result, snow-shovelling would appear to be a benign pastime when, in fact, it was lethal for some middle-aged men. For this and other similar reasons, the results of case–control studies are tenuous at best in sorting out the etiology and causation of human illness.

One final type of subexperimental study deserves mention. This is the *case series*, in which an investigator might simply report that 60% of the men who had a heart attack were shovelling snow just before the onset of their infarcts. No comparison group is provided, and about all the reader can conclude is that heart attack *can* (but not necessarily *does*) follow snow-shovelling. Such case series, though often thought-provoking, are prone to overinterpretation, especially by their investigators. In terms of strength, case series are best used to stimulate other, more powerful investigations. All too often, however, they provoke authoritarian (rather than authoritative) clinical advice about etiology, prevention and therapy.

In summary, then, readers of reports purporting to show etiology or causation should begin by deciding whether the basic methods used were strong or weak (Table I). If the basic method was a randomized trial, it is the strongest and usually can be trusted. This is how, for example, the best evidence was obtained on the real side effects produced by frequently used antihypertensive drugs.[13] A cohort analytic study, although weaker than a randomized trial, is always preferred to a case–control study, and can sometimes be trusted. Thus, the most convincing (but none the less disputed) evidence about the possible side effects of oral contraceptives comes from a large cohort study carried out by British general practitioners.[14] The case–control study is a weak design and has often led to erroneous conclusions (such as the now discredited link between reserpine and breast cancer[15]); however, for some extremely rare disorders (especially rare adverse drug reactions) we may have only case–control studies to go by and may be forced, however reluctantly, to trust them. Finally, it is not possible to tell whether any given case series can, all by itself, be trusted on an issue of etiology or causation. Thus, if other, stronger evidence is available, such case series should be passed over.

Table IV—Basic structure of a case–control study

	Outcome (heart attack)	
	Cases	Controls
Exposed*	a	b
Not exposed*	c	d

← Direction of inquiry —

*Definitions as in Table II.

Step two: Applying the diagnostic tests for causation

Having decided from the foregoing that the article warrants further consideration, readers should then turn to the Results, the Introduction and the Discussion to see how the data fit some commonsense rules of evidence. In making this causal decision, information should be sought relative to the diagnostic tests listed in Table V. They are discussed in order of decreasing importance, and we have suggested their impact upon the causal decision in Table VI.

The rules for interpreting clinical diagnostic tests that we described in an earlier round in this series (part II) can be applied here as well. For example, some of the tests for causation (such as evidence from randomized trials) are more accu-

rate than others (such as analogy). Furthermore, many of them (such as temporality) are better for "ruling out" than for "ruling in" causation. Finally, epidemiologic sense and biologic sense, although prominent in many articles, are low on the list because they have relatively low specificity; it is possible to "explain" almost any set of observations.

1. *Is there evidence from true experiments in humans?*

As we explained earlier, these are investigations in which identical groups of individuals, generated through random allocation, are or are not exposed to the putative causal factor and are followed for the occurrence of the outcome of interest.

As we have just seen, this is the best evidence we will ever have, but it is not always available and is rarely the initial evidence for causation. None the less, any consideration of an issue of causation should begin with a search for a randomized trial.

2. *Is the association strong?*

Strength here means that the odds favour the outcome of interest with, as opposed to without, exposure to the putative cause; the higher the odds, the greater the strength.

There are different strategies for estimating the strength of an association. In the randomized trial and cohort study (Tables II and III) patients who are or are not exposed to the putative cause are carefully followed up to find out whether the adverse reaction or outcome develops. Such a cohort study would, for example, compare the occurrence of impotence among ulcer patients who received cimetidine and those who did not.[2]

Cohort studies (Table III) are methodologically attractive because, like randomized trials, they permit direct calculations of strength (relative risk) by comparing outcome rates in exposed and nonexposed persons as follows:

$$\left(\frac{a}{a+b}\right) \Big/ \left(\frac{c}{c+d}\right)$$

However, as we learned in the previous section, cohort studies are often lengthy and expensive. Accordingly, the greater speed and lower cost of the case–control study (Table IV), in which patients with or without the outcome of interest (e.g., impotence) are selected and tracked backwards to their exposure to the putative cause (e.g., cimetidine), make it a much more popular approach, particularly as the first step in probing the conclusions of initial case series. Case–control or "trohoc"[16] studies pay a methodologic price for their savings in time and dollars. Strength or relative risk can only be indirectly estimated, from ad/bc. This calculation, though justified algebraically, is viewed with some scepticism.[16]

Moreover, as we have seen, case–control studies are particularly vulnerable to a series of systematic distortions (biases) that may lead to erroneous estimates of the strength of association and, therefore, incorrect conclusions about causation. Some of these biases were discussed in a previous round in this series (part III), and still others are described in detail elsewhere for readers who want to pursue this.[12]

A review of the potential effects of these biases in distorting the conclusions of case–control and cohort studies leads to two conclusions. First, case–control studies are subject to more sources of bias than are cohort studies. Second, whereas one can usually anticipate and overcome (through appropriate and rigorously applied methods) the biases affecting cohort studies, this solution is either much more difficult or impossible in the case–control strategy. As a result, readers can place considerable confidence in estimates of strength from a randomized trial, fair confidence in an estimate of strength from a cohort study and only a little confidence in an estimate of strength from a case–control study.

3. *Is the association consistent from study to study?*

The repetitive demonstration by different investigators of an association between exposure to the putative cause and the outcome of interest, using different strategies and in different settings, constitutes consistency. Thus, much of the credibil-

Table V—Step two: Applying the diagnostic tests for causation*

1. Is there evidence from true experiments in humans?
2. Is the association strong?
3. Is the association consistent from study to study?
4. Is the temporal relationship correct?
5. Is there a dose–response gradient?
6. Does the association make epidemiologic sense?
7. Does the association make biologic sense?
8. Is the association specific?
9. Is the association analogous to a previously proven causal association?

*Listed in decreasing order of importance.

Table VI—Importance of individual diagnostic tests in making the causal decision

Diagnostic test*	Effect of test result on causal decision†		
	Test result consistent with causation	Test result neutral or inconclusive	Test result opposes causation
Human experiments	+ + + +	– – –	– – – –
Strength of association			
From randomized trial	+ + + +	– – –	– – – –
From cohort study	+ + +	– –	– – –
From case–control study	+	0	–
Consistency	+ + +	– –	– – –
Temporality	+ +	– –	– – – –
Gradient	+ +	–	– –
Epidemiologic sense	+ +	..	– –
Biologic sense	+	0	–
Specificity	+	0	–
Analogy	+	0	0

*Listed in decreasing order of importance.
†+ = causation supported; – = causation rejected; 0 = causal decision not affected. The number of plus and minus signs indicates the relative contribution of the diagnostic test to the causal decision.

ity of the causal link between smoking and lung cancer arises from the repeated demonstration of a strong statistical association in case–control, cohort and other study designs.

4. *Is the temporal relationship correct?*

A consistent sequence of events of exposure to the putative cause, followed by the occurrence of the outcome of interest, is required for a positive test of temporality. Although this diagnostic test looks easy to apply, it is not. What if a second predisposing factor or a very early stage of the disorder itself is responsible for both exposure to the putative causal factor and progression to the full-blown outcome? Indeed, such an explanation might apply to studies that have linked the use of illicit stimulant or depressant drugs to the subsequent diagnosis of psychosis or depression, respectively.[17] Did the different illicit drugs cause specific forms of subsequently diagnosed mental illness, or did individuals with different subclinical but progressive mental illness seek out the specific drugs? Understandably, this yardstick is easier to apply to cohort than to case–control studies, since the latter can imply a temporal association between "exposure" and "outcome" only after both have occurred.

5. *Is there a dose–response gradient?*

The demonstration of increasing risk or severity of the outcome of interest in association with an increased "dose" or duration of exposure to the putative cause satisfies this diagnostic test. For example, in a report linking conjugated estrogens with endometrial carcinoma,[18] the relative risk of endometrial cancer rose from 5.6% among those who used the drug for 1 to 4.9 years to 7.2% among those who used it for 5 to 6.9 years and, finally, to 13.9% for those who used it for 7 or more years.

Reverse gradients are useful too. Indeed, some of the most compelling evidence of the link between cigarette smoking and lung cancer is the progressive decline in cancer risk that has been reported as previous smokers celebrate anniversaries of their last cigarette.

6. *Does the association make epidemiologic sense?*

This guide is met when the article's results are in agreement with our current understanding of the distributions of causes and outcomes in humans.

For example, Freeman,[1] reviewing the possible role of dietary fibre in the pathogenesis of colon cancer, noted several studies in which the distribution of dietary fibre among different geographic areas or populations was inversely related to the occurrence of colon cancer in the same areas and populations. Recognizing the tenuous nature of such epidemiologic correlations (after all, the declining birth rate in Europe has closely paralleled the disappearance of storks from its cities), Freeman called for "long-term prospective studies" to better define the role of dietary fibre in cancer in humans.

7. *Does the association make biologic sense?*

Is there agreement with current understanding of the responses of cells, tissues, organs and organisms to stimuli? It is with this yardstick that nonhuman experimental data should be measured. Although virtually any set of observations can be made biologically plausible (given the ingenuity of the human mind and the vastness of the supply of contradictory biologic facts), some biologic observations can be compelling, such as Himms-Hagen's description[7] of the production of massive obesity in certain strains of mice whose brown fat had only a limited capacity for thermogenesis.

8. *Is the association specific?*

The limitation of the association to a single putative cause and a single effect satisfies this diagnostic test. Examples here include some of the highly characteristic genetic disorders in which derangements in a single enzyme or another protein produce quite specific illnesses, such as hemophilia A or cystinuria. This is one of the minor diagnostic tests, being only moderately useful — and, even then, only when the illness is present. The weakness of this test is underscored when you consider that teratogens commonly have multiple effects in several organ systems.

9. *Is the association analogous to a previously proven causal association?*

The last and least of the diagnostic tests, this yardstick would link the scrotal cancer of chimney sweeps in a former era with the more recent appearance of lung cancer among persons who inhale, rather than wear, the products of combustion.

Use of these guides to reading

When confronted by a question of causation, you can use these nine diagnostic tests to distil your clinical reading and, with the assistance of judgements such as those shown in Table VI, reach a causal conclusion. Even before reading, you can use these guides to increase the efficiency of a literature search, focusing attention on the publications that will shed the strongest light on the causal question and warn against accepting plausible but biased conclusions.

Even after extensive reading and the application of all nine diagnostic tests, however, you may remain uncertain about whether, for example, drug A really causes illness B. What do you do then, and how do you translate all of this deliberation into clinical action?

We suggest that this "decision for action" has two components (Fig. 2). First is our *certainty about causation*, which is based upon the results of applying the nine diagnostic tests for causation to our clinical reading. Second is our *consideration of the consequences of the alternative courses of action* open to us (recognizing that these courses of action include noninterference as well as maintenance of the status quo). The decision for

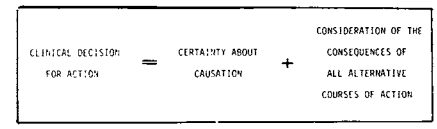

FIG. 2—Components of a "clinical decision for action".

action results from the interplay of these two components. Consider two examples:

The three reports that appeared abruptly in 1974 indicating reserpine as a cause of breast cancer[19-21] precipitated a crisis in the management of hypertension. How were we to advise and treat patients whose high blood pressure was kept under control with this drug? The first component of this decision considered the degree of certainty that reserpine did, indeed, cause breast cancer; it was never very great (in fact, the drug was later virtually pardoned by some of its earlier accusers[22]). On the other hand, the second component of this decision identified an alternative course of action that was highly attractive to many Canadian clinicians: switching appropriate patients from reserpine to propranolol. Thus, in this case even a low degree of certainty about causation was attended by the clinical decision to stop prescribing a drug for many patients because alternative treatment was available.

In contrast, the degree of certainty that oral contraceptives cause thromboembolism is much higher. None the less, oral contraceptives are still widely used. Although the reasoning behind the decision to continue oral contraceptive use in the face of growing evidence that it causes thromboembolism is complex, it is due, in part, to the second component of the decision: the consequences of alternative approaches to birth control may be judged even less desirable than the small but real risk of thromboembolism. Thus, the use of oral contraceptives continues (and, interestingly, the diagnostic test of the dose–response gradient is involved to justify the progressive reduction of certain hormonal constituents of oral contraceptives).

The diagnosis of causation is not simply arithmetical, and the strategies and tactics for making this judgement are still primitive. The diagnostic tests presented here are a start, and we suggest that their use, particularly when clearly specified before a review of relevant data, will lead to more rational — albeit less colourful — discussions of causation in medicine.

The next and final round in this series will address how to read clinical journals to distinguish useful from useless or even harmful therapy.

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BOOKS

This list is an acknowledgement of books received. It does not preclude review at a later date.

ADVANCES IN HEART DISEASE. Volume 3. Edited by Dean T. Mason. Grune & Stratton, New York; Academic Press Canada, Don Mills, Ont., 1980. $87.10. ISBN 0-8089-1284-4

AFTER THE EMERGENCY. Follow-up Instructions for Patients in English and Spanish. David B. McMicken. Spanish translations by Frank Quintero. 167 pp. EM Books, New York, 1980. $6.95, paperbound

BLOOD PRESSURE CONTROL. Volume 1. Thomas G. Coleman. 248 pp. Eden Press Inc., Westmount, PQ, 1981. $32.50. ISBN 0-88831-088-9

CHILDREN IN NEED OF SPECIAL CARE. Human Horizons Series. Thomas J. Weihs. 184 pp. Souvenir Press Ltd., London; John Wiley & Sons Canada, Limited, Rexdale, Ont., 1971. Reprinted 1980. Price not stated, paperbound. ISBN 0-285-62003-7

THE CLINICAL TRAINING OF DOCTORS. An Essay of 1793. Philippe Pinel. Edited and translated, with an introductory essay by Dora B. Weiner. 102 pp. Illust. The Johns Hopkins University Press, Baltimore, Maryland, 1981. $7.50, paperbound. ISBN 0-8018-2448-6

CPR AND EMERGENCY CARDIAC CARE: LOOKING TO THE FUTURE. The Proceedings of the New York Health Association Conference on Current Practice and Current Research in Cardiopulmonary Resuscitation and Emergency Cardiac Care. Edited by Joseph Schulger and Alan F. Lyon. 144 pp. Illust. EM Books, New York, 1980. $8.95, paperbound

continued on page 1031

Early hospital discharge and early puerperal complications

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Ramírez-Villalobos D, Hernández-Garduño A, Salinas A, González D, Walker D, Rojo-Herrera G, Hernández-Prado B. Early hospital discharge and early puerperal complications. Salud Publica Mex 2009;51:212-218.

Abstract

Objective. To evaluate the association between time of postpartum discharge and symptoms indicative of complications during the first postpartum week. **Materials and Methods.** Women with vaginal delivery at a Mexico City public hospital, without complications before the hospital discharge, were interviewed seven days after delivery. Time of postpartum discharge was classified as early (≤24 hours) or late (>25 hours). The dependent variable was defined as the occurrence and severity of puerperal complication symptoms. **Results.** Out of 303 women, 208 (68%) were discharged early. However, women with early discharge and satisfactory prenatal care had lower odds of presenting symptoms in early puerperium than women without early discharge and inadequate prenatal care (OR 0.36; 95% confidence intervals = 0.17-0.76). **Conclusions**. There was no association between early discharge and symptoms of complications during the first postpartum week; the odds of complications were lower for mothers with early discharge and satisfactory prenatal care.

Key words: patient discharge; postpartum period; postnatal care; Mexico

Ramírez-Villalobos D, Hernández-Garduño A, Salinas A, González D, Walker D, Rojo-Herrera G, Hernández-Prado B. Egreso temprano postparto y complicaciones en el puerperio mediato. Salud Publica Mex 2009;51:212-218.

Resumen

Objetivo. Evaluar la asociación entre el tiempo de egreso posparto y las posibles complicaciones en el puerperio mediato. **Material y métodos.** Mujeres con parto vaginal atendidas en un hospital público de la Ciudad de México, sin complicaciones antes del egreso hospitalario**,** fueron entrevistadas a los siete días de egreso. La variable dependiente fue la ocurrencia y severidad de complicaciones. Se calcularon media y desviación estándar para las variables continuas, y proporciones para las categóricas. Las variables relacionadas con egreso temprano en el análisis bivariado (con $p<0.15$) fueron incluidas en un modelo de regresión logística. **Resultados.** Se analizó información de 303 partos, de los cuales 208 (68%) tuvieron egreso temprano posparto. Las mujeres que fueron egresadas en forma temprana con un control prenatal adecuado reportaron menos síntomas de complicaciones en el puerperio mediato (RM= 0.36; IC 95% = 0.17-0.76). **Conclusiones.** Aunque no se encontró asociación entre el egreso temprano y los síntomas de complicaciones durante la primera semana del posparto, el riesgo de complicaciones fue menor en mujeres con egreso temprano y con cuidado prenatal adecuado, comparadas con las mujeres que presentaron egreso tardío sin control prenatal.

Palabras clave: alta del paciente; periodo de posparto; atención posnatal; México

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In recent years, there has been growing interest to determine the ideal time for postpartum discharge for optimal maternal and child outcomes.[1-9] Hospital length of stay after childbirth has decreased progressively during the past 60 years.[10-15] In the early 1980s in Mexico, the Mexican Social Security Institute (Instituto Mexicano del Seguro Social – IMSS) developed the program *Atención de Parto de Bajo Riesgo* (Care for Low-Risk Delivery),[16, 17] which resulted in a six-hour reduction in postpartum hospital stays.

For women who have uncomplicated vaginal deliveries, the American College of Obstetrics and Gynecology (ACOG) defines early discharge (ED) as a hospital stay lasting 48 hours or less, and considers a stay of 24 hours or less very early discharge (VED).[18-21] The hypothesis of this study is that shorter postpartum stays are associated with poor health outcomes because of the decreased probability of detecting postpartum complications, as has been found in studies with other populations.[22]

Little information is available in Mexico to assess the potentially negative effects of early hospital discharge on maternal health during early puerperium, defined as the period between 24 hours to 7 days postpartum.[23] It is important to assess whether mothers who are discharged early after vaginal delivery are at risk to develop complications, as well as what type of complications may occur. The aim of this study was to evaluate the association between time of postpartum discharge and reported symptoms indicative of complications during early puerperium.

Material and Methods

The study population consisted of women who received obstetric care after normal vaginal delivery at the Gynecology and Obstetrics Department of the General Hospital of Mexico (HGM), Mexico City, Ministry of Health (Secretaría de Salud, SSA) between April and December 2003.

The inclusion criteria for the study were: a) vaginal delivery of a live singleton term infant (gestational age 37 to 41 weeks); b) uncomplicated pregnancy without concomitant diseases such as diabetes, hypertension, preeclampsia, cardiopathy, epilepsy, or evident infections; c) routine postpartum care, and d) residence in Mexico City. The exclusion criteria were refusal to participate, checking out of the hospital separately from the child and residing outside the city. The withdrawal criteria were refusal to continue participating and failure to locate the patient after three attempts.

Six trained interviewers evaluated medical records to select subjects who fulfilled the inclusion criteria and then invited eligible mothers to participate in the study. After signed informed consent, selected mothers participated in a face-to-face interview prior to leaving the hospital to collect the following baseline data: a) sociodemographic characteristics; b) gynecologic and obstetric history; c) prenatal care assessed according to the Official Mexican Norm (NOM-007-SSA2-1993),[24] d) delivery events, including vaginal lacerations; e) clinical characteristics of the immediate puerperium, (considered as the 24-hour period following delivery);[24] and f) physician's discharge orders. A chart review was performed for all cases to corroborate questionnaire data and obtain clinical information. Upon discharge, mother-child pairs were invited for a medical visit seven days after delivery to assess newborn health status. At this visit, mothers underwent another face-to-face interview to obtain information related to maternal and infant postpartum health.

Women reporting serious complication symptoms were referred to the hospital's Gynecology and Obstetrics Service for clinical evaluation. In the event that the mother failed to attend the 7-day follow-up appointment, a trained interviewer visited her at home to complete the interview. The study was approved by the Ethics, Biosafety, and Research Committees of the Mexican National Institute of Public Health and of the General Hospital of Mexico.

The study outcome variable was the presence of self-reported symptoms in early puerperium. This variable was measured using symptoms reported by the mother during an interview conducted seven days after hospital discharge. Symptoms were categorized as suggestive of: a) urinary tract infection (dysuria, frequent urination, bladder tenesmus); b) episiotomy complications (local pain or discomfort, bleeding, separation of sutures, c) episiotomy infection (purulent discharge, pain, warmth and redness in the area); d) endometritis: (uterine pain, foul smelling lochia, and fever or shivering); f) mastitis and/or mammary abscess (pain, heat, and redness or cracking of nipples); and g) other reported symptoms or hospital readmission. Subjects were assigned one of two categories: a) absence of symptoms or b) presence of any symptom.

The exposure variable was the time of postpartum hospital discharge, measured as the time elapsed from delivery to hospital discharge (according to hospital records). For this study, early postpartum discharge (ED) was defined as 24 hours or less, whereas late discharge (LD) was defined as later than 25 hours. Potential confounders included sociodemographic or obstetric variables, perinatal and delivery events, and early postpartum complications.

It is important to clarify that in the facility where the study was conducted, physicians' discharge orders

are given by the responsible obstetrician during clinical rounds that occur each day in the morning and afternoon. Depending on the clinical status of the patient the rounding physician will give the discharge order. These orders depend on non-clinical (bill must be paid prior to discharge and dedicated blood donation is sometimes required) as well as clinical (no apparent complication) indications for discharge. In some cases of non-clinical discharge, some women in the late discharge group were actually candidates for early discharge but were kept for non-clinical reasons.

Statistics

Data are presented as mean and standard deviation for continuous variables and proportions for categorical variables. Bivariate associations between the outcome variable and each of the covariates were assessed to obtain odds ratios and 95% confidence intervals. The variables related to early discharge in the bivariate analysis at $p<0.15$ were included in a logistic regression model.

An interaction term was added to assess the potential modifying effect of ED with satisfactory prenatal care on the presence of complications in early puerperium. All women with any complication identified during the hospital stay were excluded from the analysis. There were four women whose hospital stays were longer than 72 hours (77, 79, 87 and 99 hours). The analysis was conducted both including and excluding those observations, and no differences were found. The results that we present in this paper include these four women.

Finally, regression diagnostics were obtained for the logistic model.[25] The statistical analysis was performed using Stata Version 9.0.*

Results

Of the 5 326 women who delivered at the HGM between April 11 and December 15, 2003, a total of 2 710 (50.8%) had normal vaginal deliveries; 829 of those were eliminated due to premature birth, low birth weight (≤2 600 g or ≤36 weeks gestational age), stillbirths, or twins. Of the remaining 1 881 vaginal deliveries, 1 216 (64.6%) fulfilled all inclusion criteria. Of these women, 323 (26.6%) did not participate because they resided outside the metropolitan area or simply because they did not wish to participate in the study. No differences were found between women who agreed to participate and those who did not with respect to number of live born children, newborn weight, maternal age or time of discharge. From the 893 remaining women, 497 were excluded from the analysis because they had complications before the hospital discharge. Out of the 396 women without complications prior to hospital discharge, only 303 were included in the analysis because 93 did not have complete information on the variables under study (Figure 1). We did not find significant differences between women with complete and incomplete information regarding their age, length of hospital stay and number of live-born children.

During follow-up, 63 women (15.9%) were lost due to change of residence, failure to locate the place of residence after three attempts, or incorrect address. No significant differences were found between women who completed the study and those who were lost to follow-up, regarding the length of hospital stay, age, and number of live-born children.

A total of 303 mothers were included in the analysis. Almost two thirds (67.2%) were interviewed at the hospital appointment while 32.8% were interviewed at home. Among these women, 208 (68.6%) had early postpartum discharge and 62 (15.6%) had their discharge delayed for administrative reasons; of these, 14 (6.7%) were in the late discharge group. There were no differences found in age or length of hospital stay between women with delayed discharge due to administrative reasons and those without this delay.

Table I shows sociodemographic and delivery characteristics of participating women, by time of discharge. The mean hospital stay (HS) was 21.5 ± 8.5 hours.

Table II presents symptoms reported up to the seventh day postpartum, analyzed from the time of discharge. From the 303 women included in the analysis, 65% (215) reported at least one symptom after hospital discharge. The most frequent symptom was genital discomfort, which was reported by 26.9% of the women, followed by symptoms suggesting urinary tract infection (23.1%) and symptoms suggesting endometritis (3.4%). We found no significant differences in the occurrence of each of the signs and symptoms by time of discharge (Table II). One woman was hospitalized on the fifth day after delivery with fever.

We fit a multivariate logistic regression model with the dependent variable being the presence of symptoms and the covariates being age of the mother in years, number of live-born children, admission in the second stage of labor, satisfactory prenatal care, application of enema prior to the delivery and having received instructions to have a medical check-up seven days after

* StataCorp LP. Stata Statistical Software STATA/SE for Windows; Release 9.0, Special Edition. College Station (TX, USA): Stata Corporation, 2002.

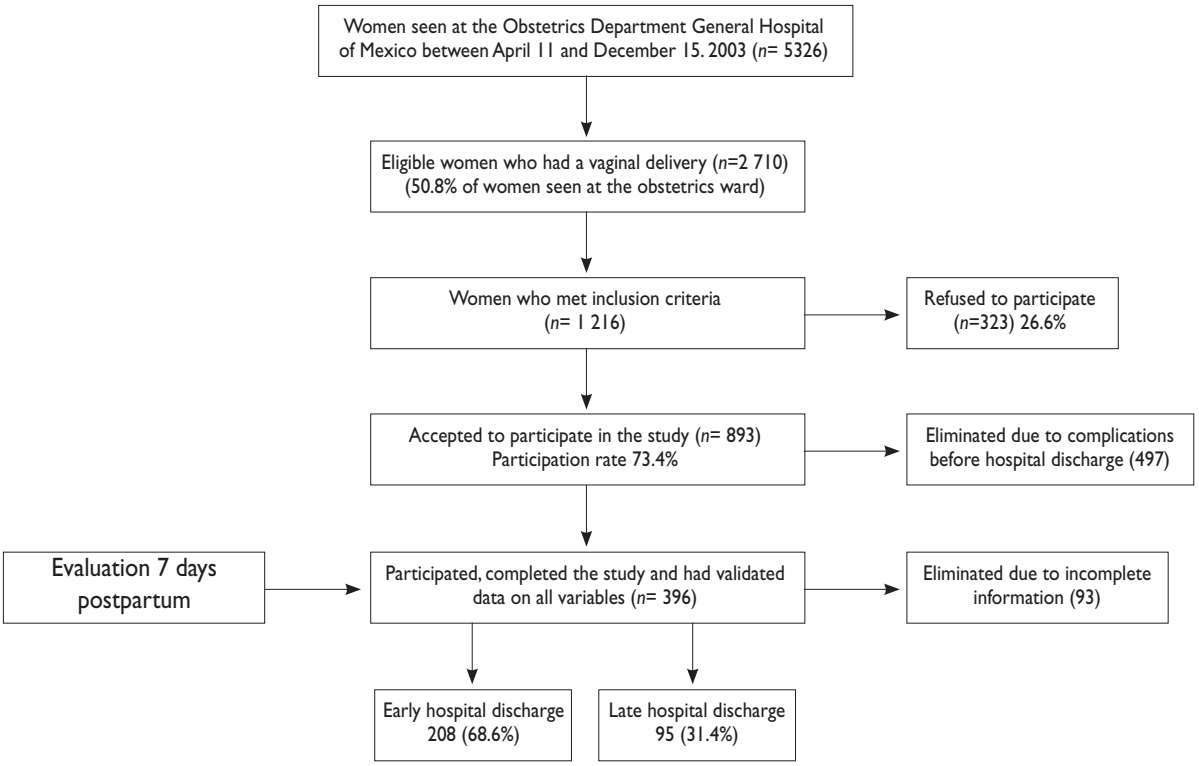

FIGURE 1. FLOWCHART FOR RECRUITMENT AND FOLLOW-UP AFTER VAGINAL DELIVERY. GENERAL HOSPITAL OF MEXICO, MEXICO CITY, MEXICO, 2003

delivery. The analysis also included the time between maternal discharge from the hospital and the day on which the interview was conducted. The results are shown in Table III.

The raw analysis did not find any variable associated with the presence of early puerperium complications. The analysis adjusted for confounding variables found that women who received no instructions to have a medical check-up seven days after delivery had a higher odds ratio of reporting symptoms of complications than women who received follow-up instructions (*OR* 1.73; 95% CI 1.01. 2.97). Early discharge was not associated with the presence of symptoms during early puerperium. Nevertheless, in the adjusted models with interaction terms between early discharge and satisfactory prenatal care, we found that women with early discharge and satisfactory prenatal care had a 63% lower odds of presenting symptoms compared with women with late discharge and whose prenatal control was unsatisfactory.

Discussion

This study found no significant association between early discharge and maternal symptoms of complications during the early puerperium. This result is consistent with other investigators such as Brown *et al*.[12] We found that women who had satisfactory prenatal care and early discharge had lower odds ratio of presenting symptoms of complications than mothers who had early discharge but whose prenatal care was not satisfactory. This study also found that women who received no instructions to get a medical check-up after discharge had a higher risk of presenting complications, what may be an indicator of a positive effect of counseling during the hospital stay.

The association between prenatal care and reported symptoms can be interpreted in the following manner: satisfactory prenatal care serves as an important venue for educating women about postnatal care and their own health;[24-26] prenatal visits can help resolve mothers'

Table I

Characteristics describing mothers studied according to time of postpartum hospital discharge. General Hospital of Mexico. Mexico, 2003

Variable	*Early discharge (≤24 hrs) n (%) 208 (68.6)*	*Late discharge (≥25 hrs) n (%) 95 (32.4)*
Duration of hospital stay	17.2	32.4
Maternal age (years)	22.8*	23.2
14-19	70 (33.6)	27 (28.4)
20-34	134 (64.4)	62 (65.3)
≥35	4 (1.9)	6 (6.3)
Marital status		
Single‡	170 (81.7)	79 (83.2)
Having a partner	38 (18.2)	16 (16.8)
Education level		
None	0	1 (1.1)
Elementary school completed	46 (22.2)	33 (34.7)
Middle school completed	113 (54.3)	45 (47.4)
High school or more	49 (23.5)	16 (16.8)
Obstetric history		
Prenatal care		
Satisfactory#	70 (33.6)	367 (37.9)
Unsatisfactory	138 (66.4)	59 (56.1)
Number of live-born children		
Primigravida	10 (4.8)	9 (9.5)
2-3	99 (47.6)	49 (51.6)
4 or more	99 (47.6)	37 (38.9)
Status of the patient at the time of admission		
Second stage	20 (9.6)	11 (11.6)
Ruptured membranes	26 (12.8)	15 (16.3)
Active labor	162 (94.2)	80 (97.6)
Procedures		
Labor induction	11 (5.4)§	13(14.3)§
Application of enema	43 (20.7)	19 (20.0)
Episiotomy	164 (79.6)	63 (67.9)
Revision of uterine cavity after delivery	207 (99.5)	93 (98.9)
Bladder catheter at the time of delivery	117 (62.2)	46 (53.5)
Type of anesthesia		
None or local	115 (55.3)	44 (46.7)
Epidural	93 (44.7)	51 (53.6)
Receiving instructions to attend a check-up seven days after delivery	52 (60.5)	34 (39.5)

* Mean (SD)
‡ Single, separated, divorced or widowed women
§ Observations made with missing data
# Satisfactory prenatal care according to the Mexican Official Norm NOM-007-SSA2-1993

doubts about events during puerperium as well as provide instructions for when to seek medical care;[27,28] early postpartum discharge (EPD) can reduce the window of opportunity for detecting potential complications and for counseling the mother on puerperal care, especially if she did not receive satisfactory prenatal care. It is important to note that even with early discharge, women with satisfactory prenatal care had lower odds of complications than women without early discharge and unsatisfactory prenatal care. This finding indicates that prenatal care plays an important role not only in the prevention of prenatal and delivery complications, but also serves to educate the mother as to early postpartum care.

There are a number of limitations of this study that deserve mentioning. The data on the presence and severity of symptoms of complications during early puerperium were obtained by interviewing the mothers and not by clinical exam or evaluation, which may lead to errors in classification. Also, we did not determine the reasons why mothers did not seek medical attention despite complaining of certain symptoms. However, we presume that the problems in detection and identification of these symptoms, as well as the reasons for not seeking medical care despite the presence of symptoms, are not related to the time of postpartum discharge. This would likely result in a non-differential error in measurement and would only attenuate the associations found between time of postpartum discharge and the occurrence of complications.

Recall bias may be another limitation of this study, as mothers simply tried to remember symptoms when the survey was administered. However, the authors contend that if such bias were present it also would be non-differential, given that mothers were all asked in the same manner (regardless of early or late discharge). Another limitation of the study is the short follow up period of only seven days. Although the majority of the symptoms identified here occur preferentially during the first week postpartum, it is possible that other symptoms or complications appeared after those seven days and were not identified or analyzed, but this issue is part of a future complementary analysis.

In the present study, early discharge was decided by the responsible physician. Women in the early discharge group were all clinically stable. However, for administrative reasons, some women who would have been candidates for early discharge were kept in the hospital. Although it is impossible to control for this effect, we included this "late discharge for administrative reasons" variable in the model and found no significant attributable effect.

The ideal design for evaluating the association between the time of discharge postpartum and the pres-

Table II

SYMPTOMS REPORTED BY MOTHERS DURING EARLY PUERPERIUM, BY TIME OF HOSPITAL DISCHARGE. GENERAL HOSPITAL OF MEXICO. MEXICO, 2003

Symptoms reported at seven days postpartum	*Early discharge group n = 208 (%)*	*Late discharge group n = 95 (%)*	*Crude OR**	*95% CI*
Symptoms of urinary tract infection[‡,§]	48 (23.1)	21 (22.1)	1.05	0.59, 1.89
Genital discomfort (pain and edema of labia)[§]	56 (26.9)	18 (18.9)	1.57	0.86, 2.86
Breast conditions (abscess, mastitis)	2 (0.96)	0	-	-
Symptoms infection at the site of episiotomy[#]	24 (11.5)	9 (9.5)	1.24	0.55, 2.79
Symptoms of endometritis[§,&]	7 (3.4)	1 (1.05)	3.37	0.39, 26.98
Hospital readmission	1 (0.48)	0	-	-

* Binary logistic regression
‡ Dysuria, frequent urination and vesical tenesmus
§ Missing data in one observation
# Pus or dehiscence, episiotomy or cellulitis in episiotomy site
& Uterine pain along with fever or shivering

Table III

LOGISTIC REGRESSION MODEL. FACTORS ASSOCIATED WITH COMPLAINTS OF COMPLICATIONS DURING EARLY PUERPERIUM AND THE DIFFERENTIAL EFFECT OF EARLY DISCHARGE. GENERAL HOSPITAL OF MEXICO. MEXICO, 2003

Variables	*OR Crude analysis*		*OR Adjusted analysis**		*OR Adjusted with Interaction**	
	OR	*95% CI*	*OR*	*95% CI*	*OR*	*95% CI*
Early discharge	0.62	0. 37, 1.02	0.54	0.31, 0.94	0.95	0.41,2.20
Age (years)	1.00	0.96, 1.04	0.99	0.94,1.05	0.99	0.94,1.04
Two or more children	1.22	0.56, 2.68	1.13	0.45, 2.81	1.13	0.45,2.84
Admission in the second stage of labor	1.56	0.67, 3.63	1.46	0.61, 3.47	1.42	0.59,3.38
Application of enema	0.78	0.44, 1.40	0.78	0.43, 1.42	0.80	0.44,1.46
Not receiving instructions to attend medical check-up seven days after delivery	1.57	0.94, 2.64	1.69	0.99, 2.8	1.73	1.01,2.97
Satisfactory prenatal care	0.84	0.51, 1.38	0.82	0.49, 1.35	0.41	0.16, 1.05
Interaction between early discharge with satisfactory prenatal care					0.36	0.17,0.76

* Adjusted for the variables in the table, the time elapsed since discharge and interview data

ence of complications would be a randomized clinical trial instead of the cohort observational design used in our study. Such a design would randomize women to early or late discharge groups, and clinical assessment and follow-up would yield more accurate data on puerperal complications. Due to ethical and logistic reasons, it was not possible to use such design in this report.

There may be a residual effect of complications in the immediate postpartum period, which may increase the time to discharge as well as increase the probability of complications appearing during early puerperium. Thus, the results of this study may overestimate the association between early postpartum discharge and the presence and severity of puerperal complications. To decrease the possible bias, we opted for the restriction of the study sample to only those women with no complications at the time of discharge and those with puerperal complications after delivery and before

hospital discharge, which could considerably affect the time of postpartum discharge and the probability of later complications.

The results of this study show that although there was no association between early discharge and the severity of complications during early puerperium for all mothers, the presence of symptoms decreased among women who received indications to have a medical check up one week later, and among women with early discharge and satisfactory prenatal care, compared with those with early discharge and unsatisfactory prenatal care, suggesting a positive effect of satisfactory prenatal care even with an early discharge. This correlation deserves further study in order to better understand its importance.

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